

Polybrominated Flame Retardants (PBDEs) With an Emphasis on deca BDE

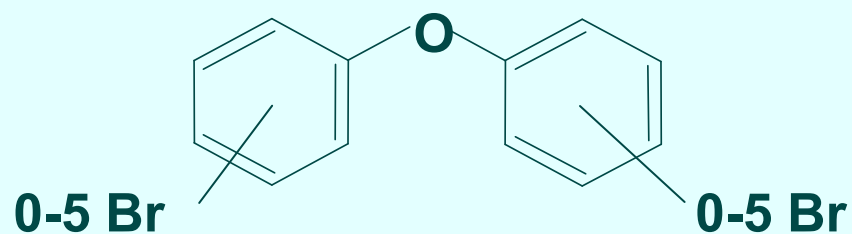
Deborah C. Rice, Ph.D.

Environmental and Occupational Health Program

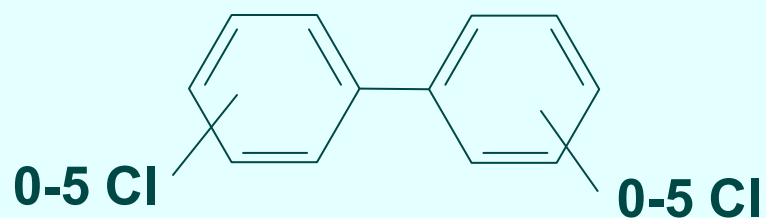
Maine Center for Disease Control and Prevention

Augusta, ME

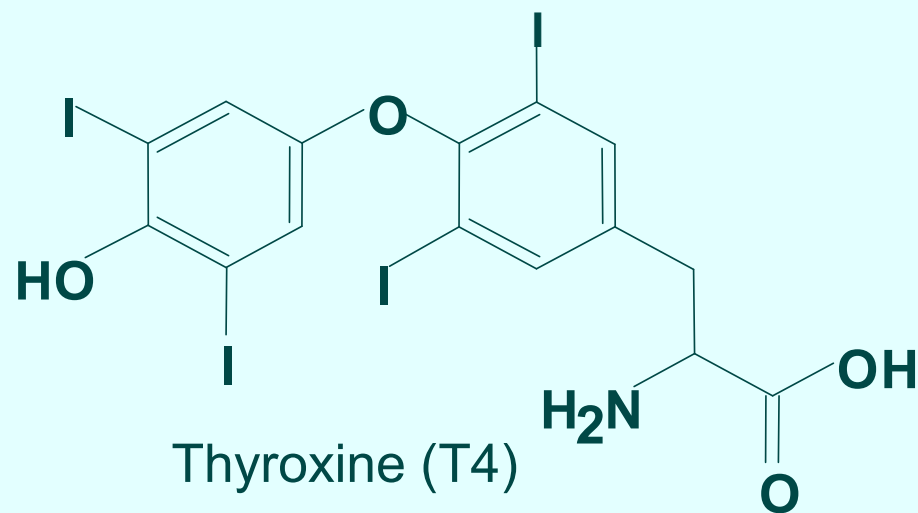
PCBs and PBDEs Have Similar Structures



Polybrominated diphenyl
ethers (PBDEs)



Polychlorinated biphenyls (PCBs)



Characteristics of PCBs

Persistent in the environment and transported long distances

Bioaccumulate and bioconcentrate up the food web

Toxic

- carcinogenic
- immunotoxic
- endocrine disruptors (including thyroid)
- developmental neurotoxins
- developmental toxicants
- reproductive toxicants
- hepatotoxic
- large database, including humans

◆ **Banned in late 1970s**

PBDEs: Failure of Regulation

- ◆ Structure of PBDEs should have triggered extensive testing before use
- ◆ No federal regulatory mechanism
- ◆ Toxic Substances Control Act (ToSCA), 1976
 - industry is not required to generate data
 - EPA has to have “substantial evidence” of “unreasonable risk” to require testing
 - EPA is required to analyze risks and benefits of all less burdensome regulatory alternatives before banning chemical, as well as risks of all substitute products
- ◆ 62,000 chemicals in production in 1979, 200 new chemicals/year
- ◆ 5 chemicals banned under ToSCA

Characteristics of PBDEs

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Bioaccumulate and bioconcentrate up the food web

Toxic

- developmental neurotoxicants
- carcinogenic
- endocrine disruptors (thyroid)
- reproductive toxicants
- hepatotoxic
- limited database, animals

◆ **Used beginning in 1970s**

Use of PBDEs

◆ Commercial penta mixture

- mainly PeBDE and TeBDE, some HxBDE
- textiles, polyurethane foam, resins

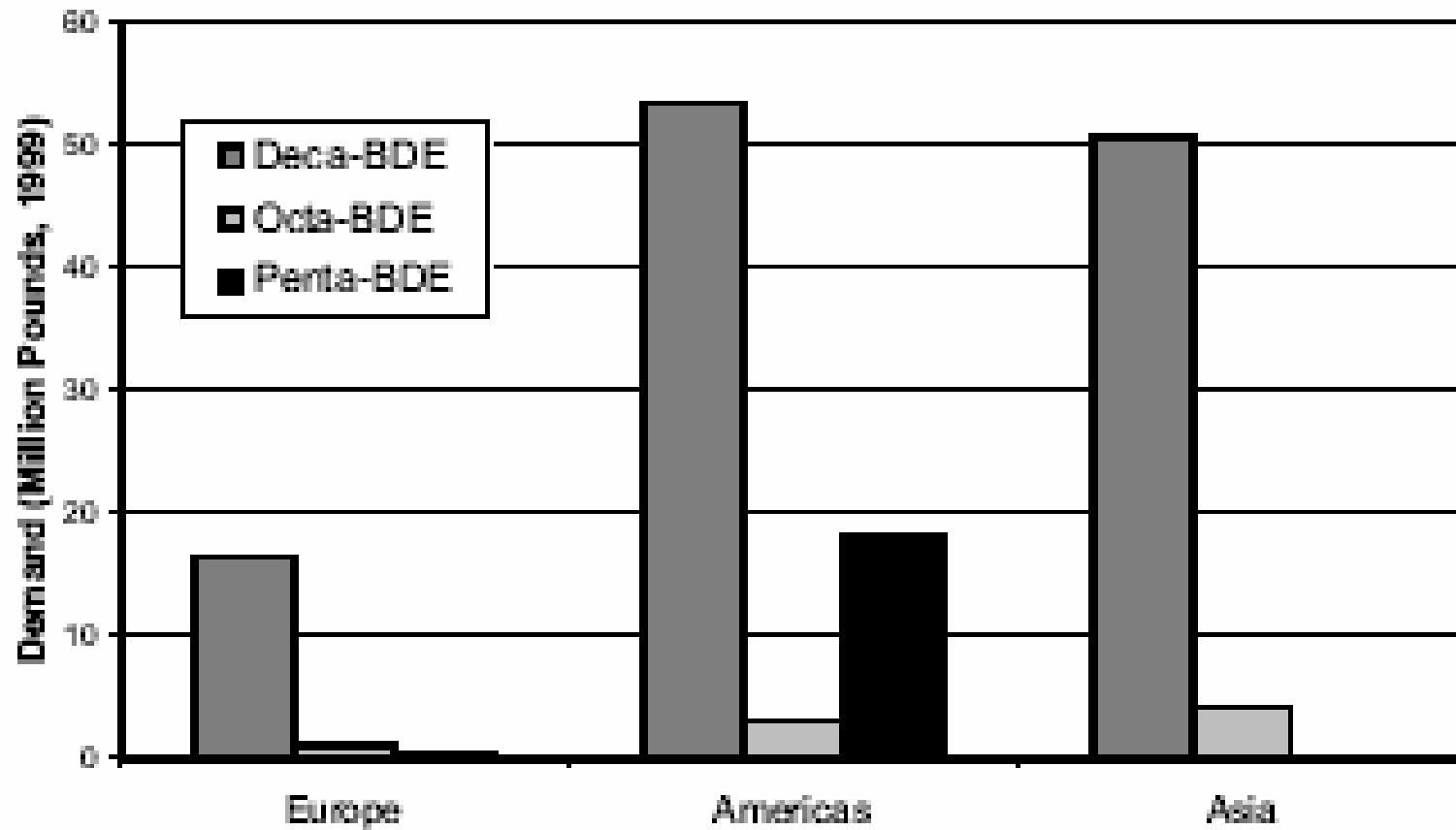
◆ Commercial octa mixture

- 6% HxBDE, 42% HpBDE, 36% OBDE, 13% NBDE, 2% DBDE
- additive in polymers for plastic housing, office equipment

◆ Commercial deca mixture

- 97% deca, 3% nonaBDE
- TV casings primarily (80% of deca use)
- textile backing
- electrical parts and wires

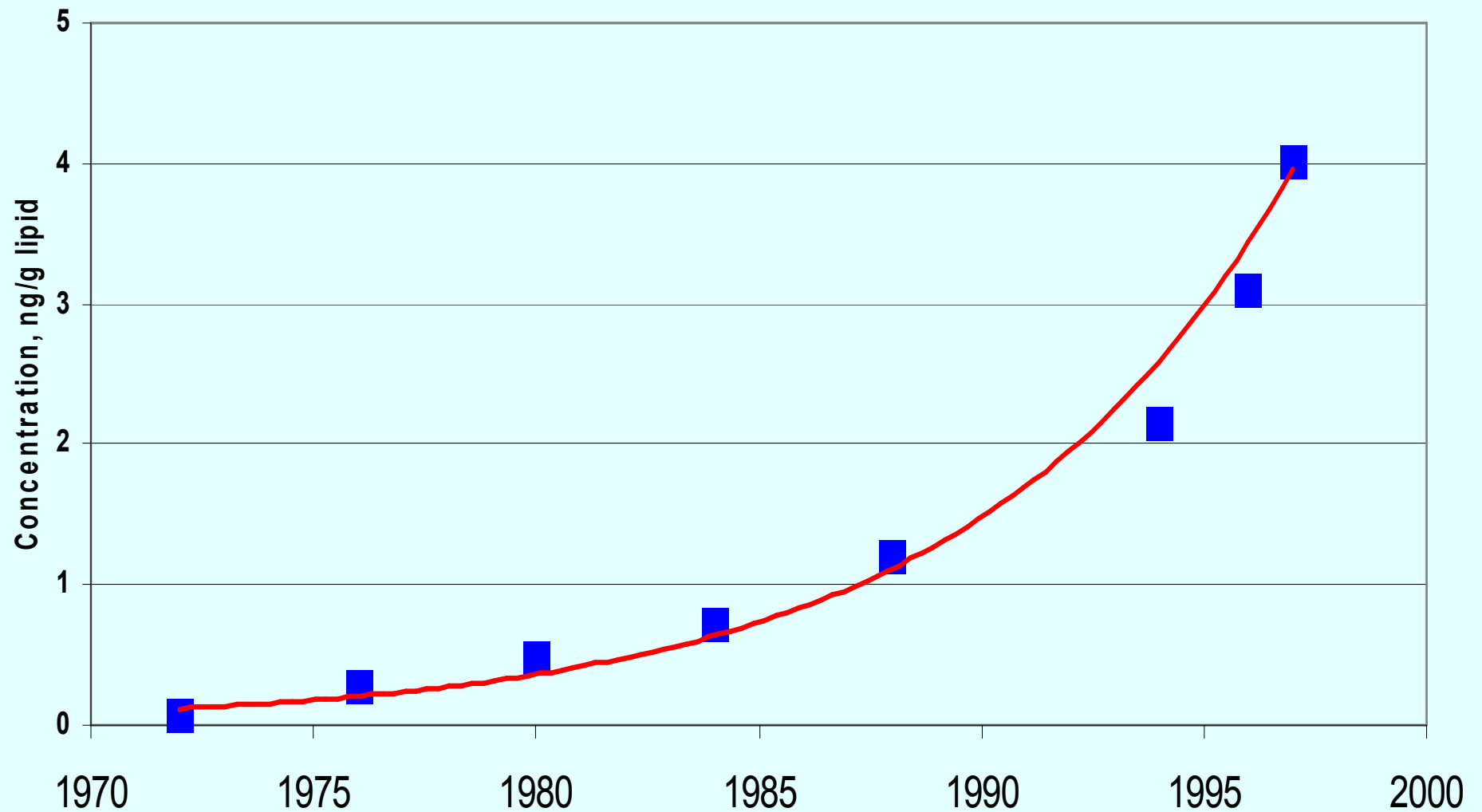
World Demand for PBDEs



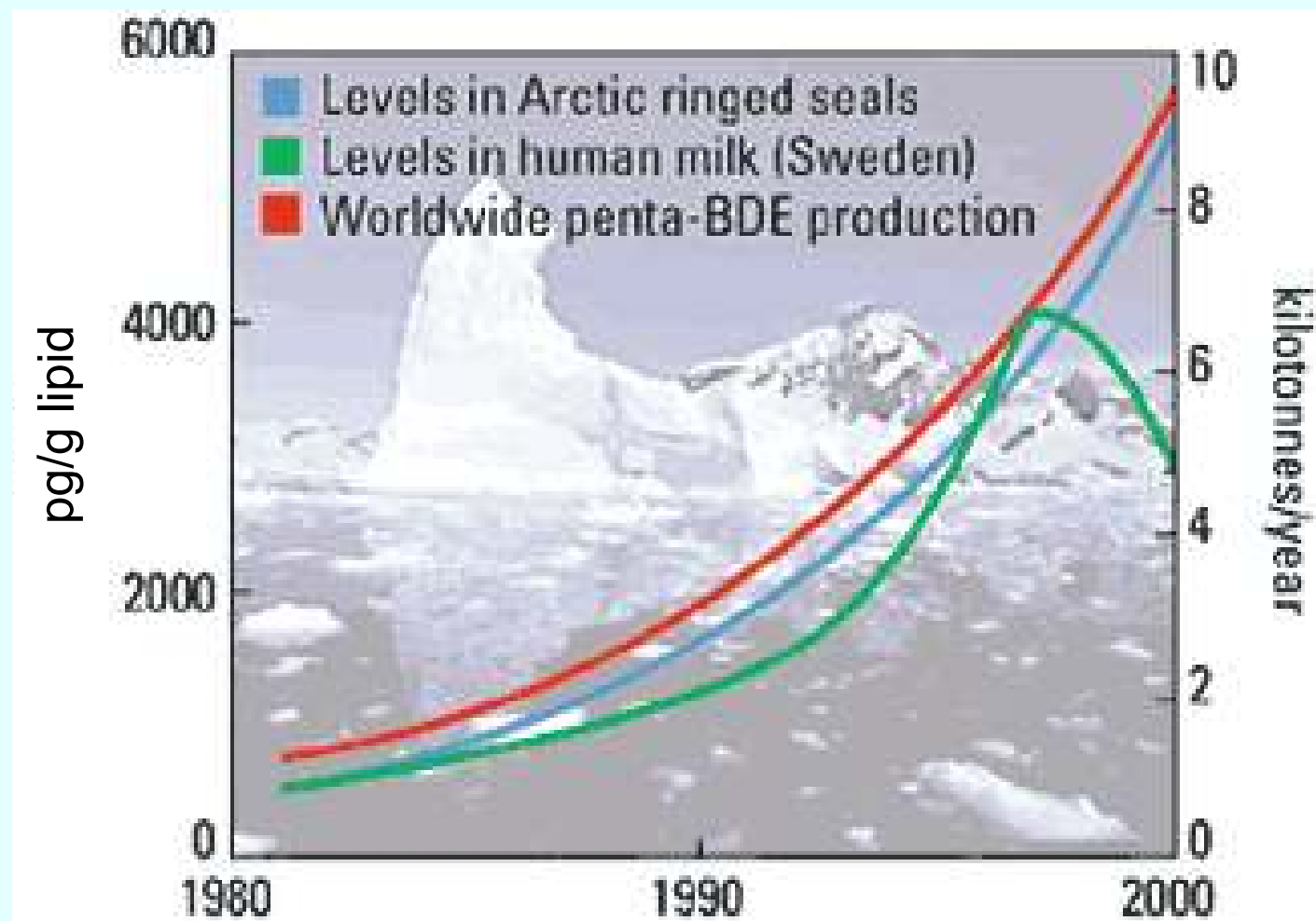
PBDE Levels in Humans

- ◆ Levels in humans in the U.S. highest in the world
- ◆ Levels in humans have increased exponentially since the 1970s
- ◆ Excreted into breast milk
- ◆ Cross the placenta

Total PBDEs, Swedish Milk Study

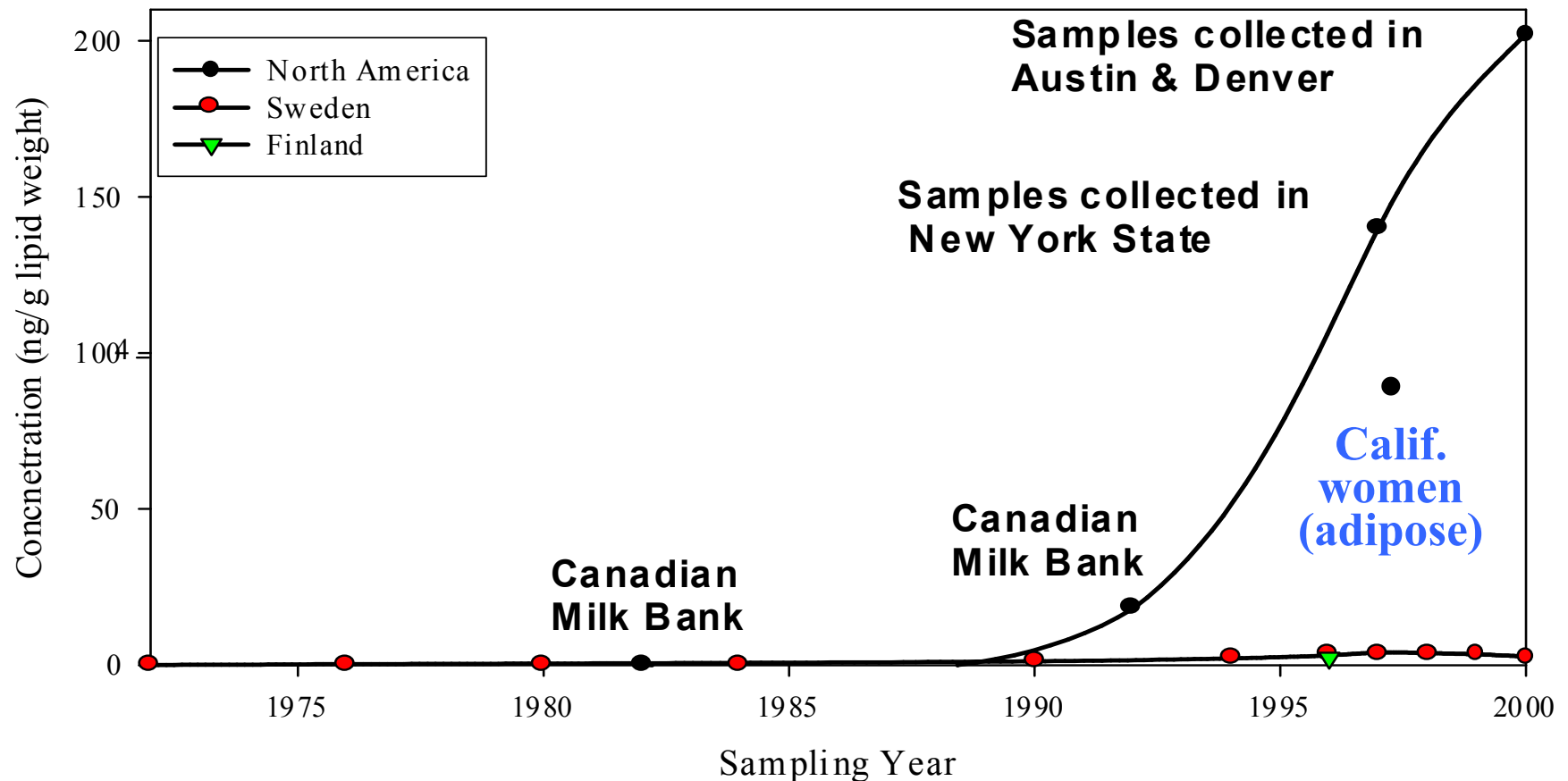


Norén & Meironyté, 1998



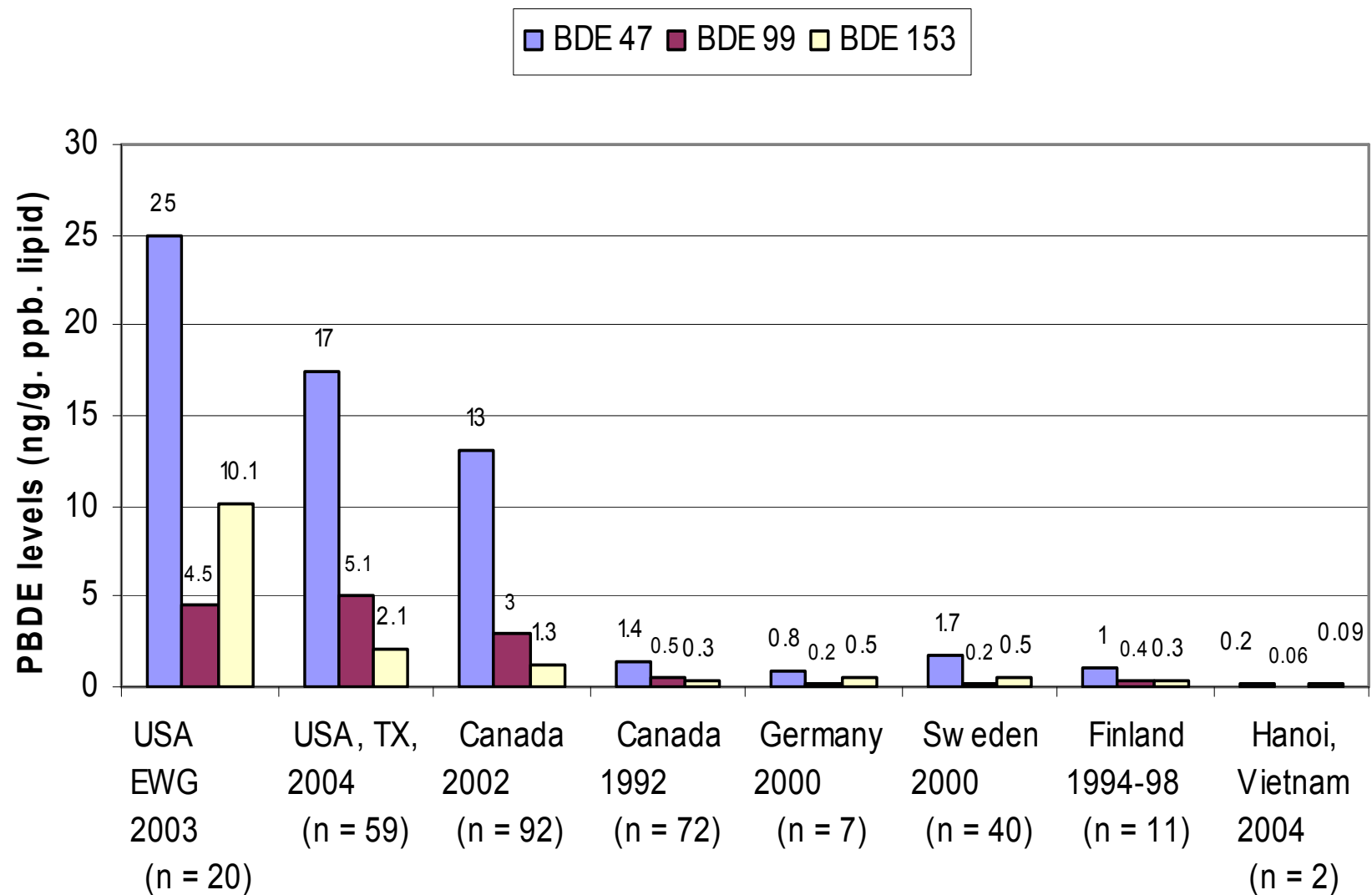
Environ. Sci. Technol. 2002

Comparison Between Concentrations of PBDEs in Breast Milk From North America and Europe

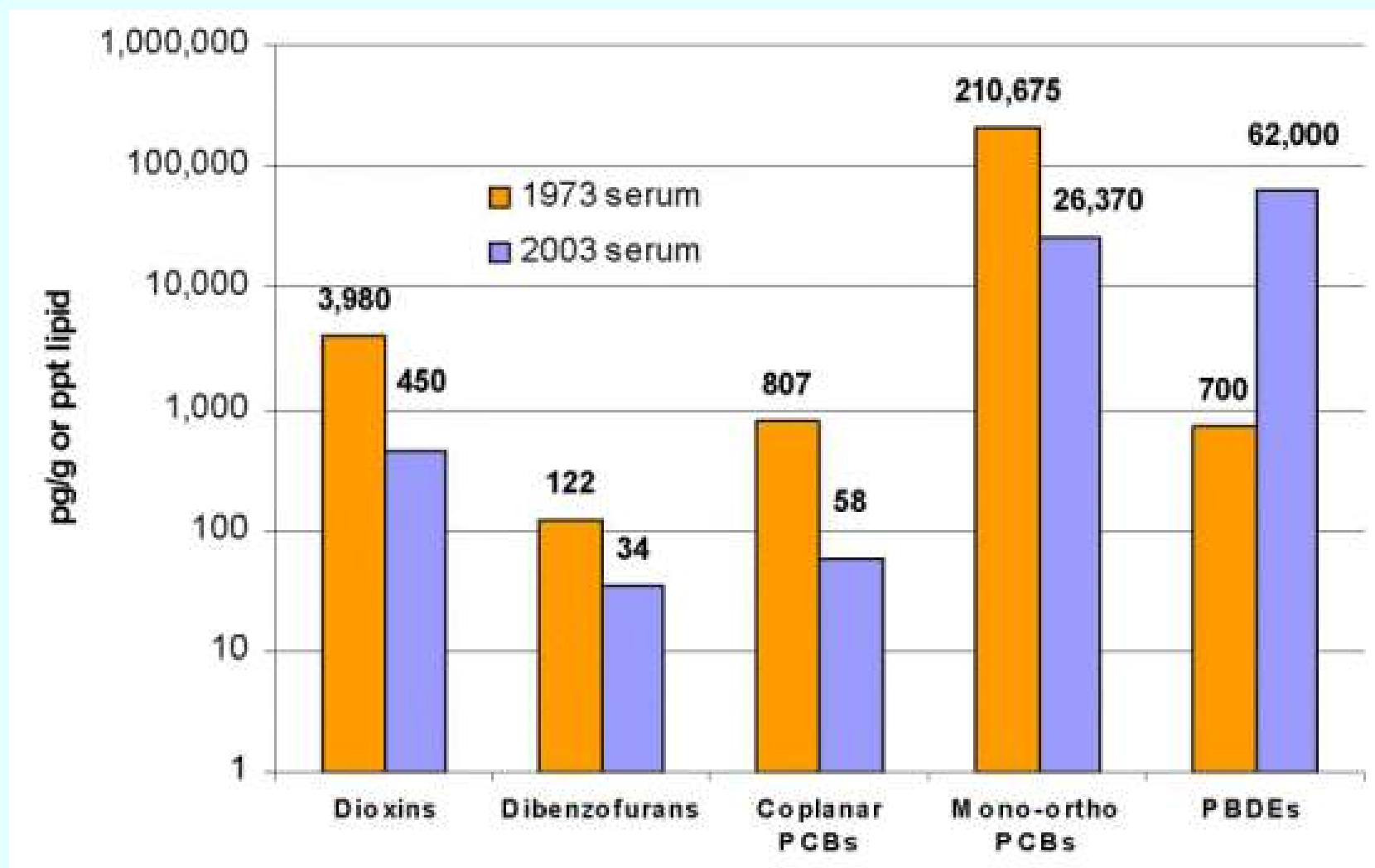


Canadian Milk Bank and New York State from Ryan and Patry 2000, Denver and Austin results from Papke et al 2001; Swedish data from Meironyte Guvemius and Noren 2001, Finnish data from Strandman et al. 2000

Median Levels of PBDE 47, 99, 153 in Human Milk from Different Countries



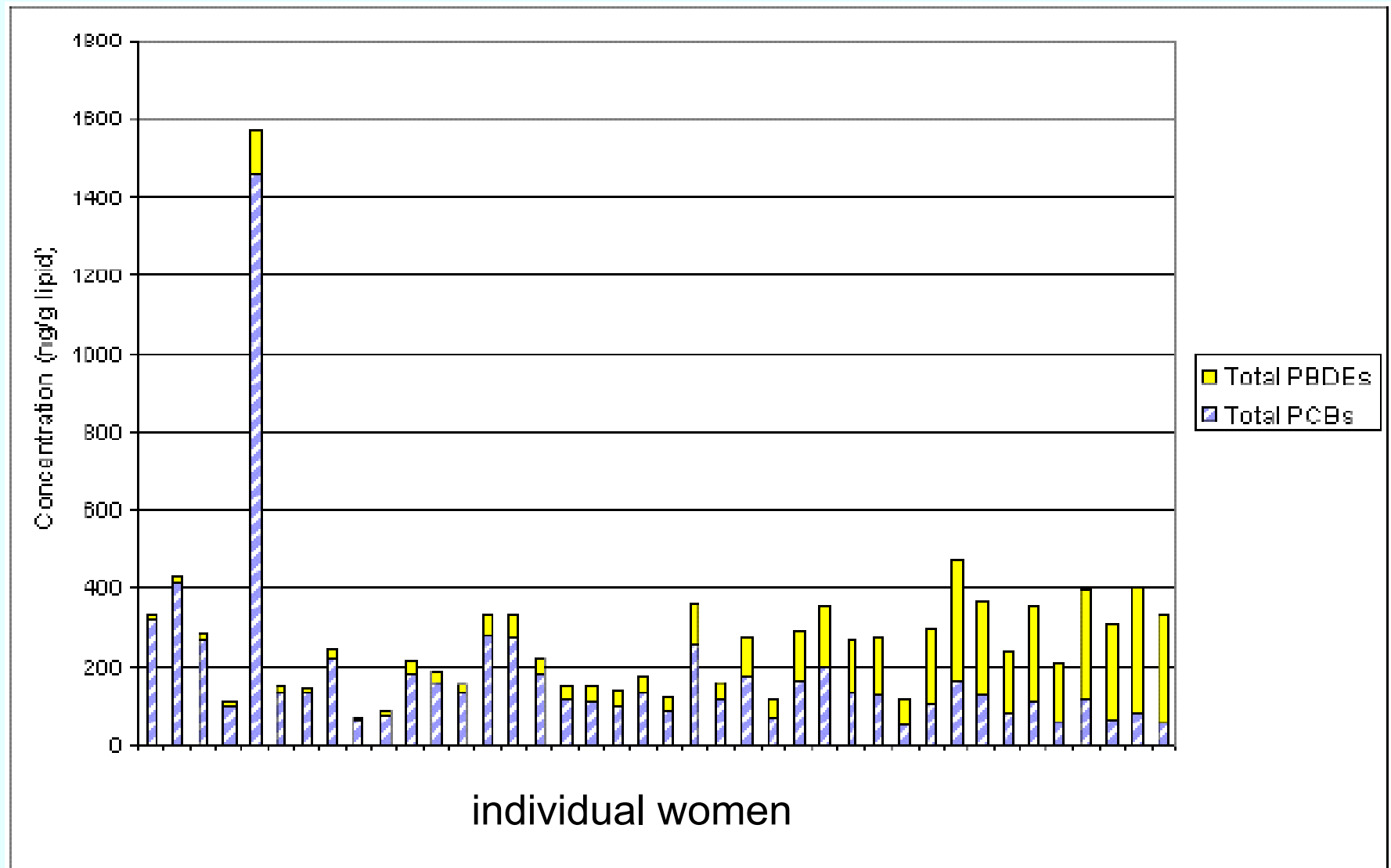
U.S. Serum Levels of Dioxins, Dibenzofurans, PCBs and PBDEs, 1973 and 2003



Schechter *et al.*

Total PBDEs and PCBs in Pacific Northwest Breast Milk Samples

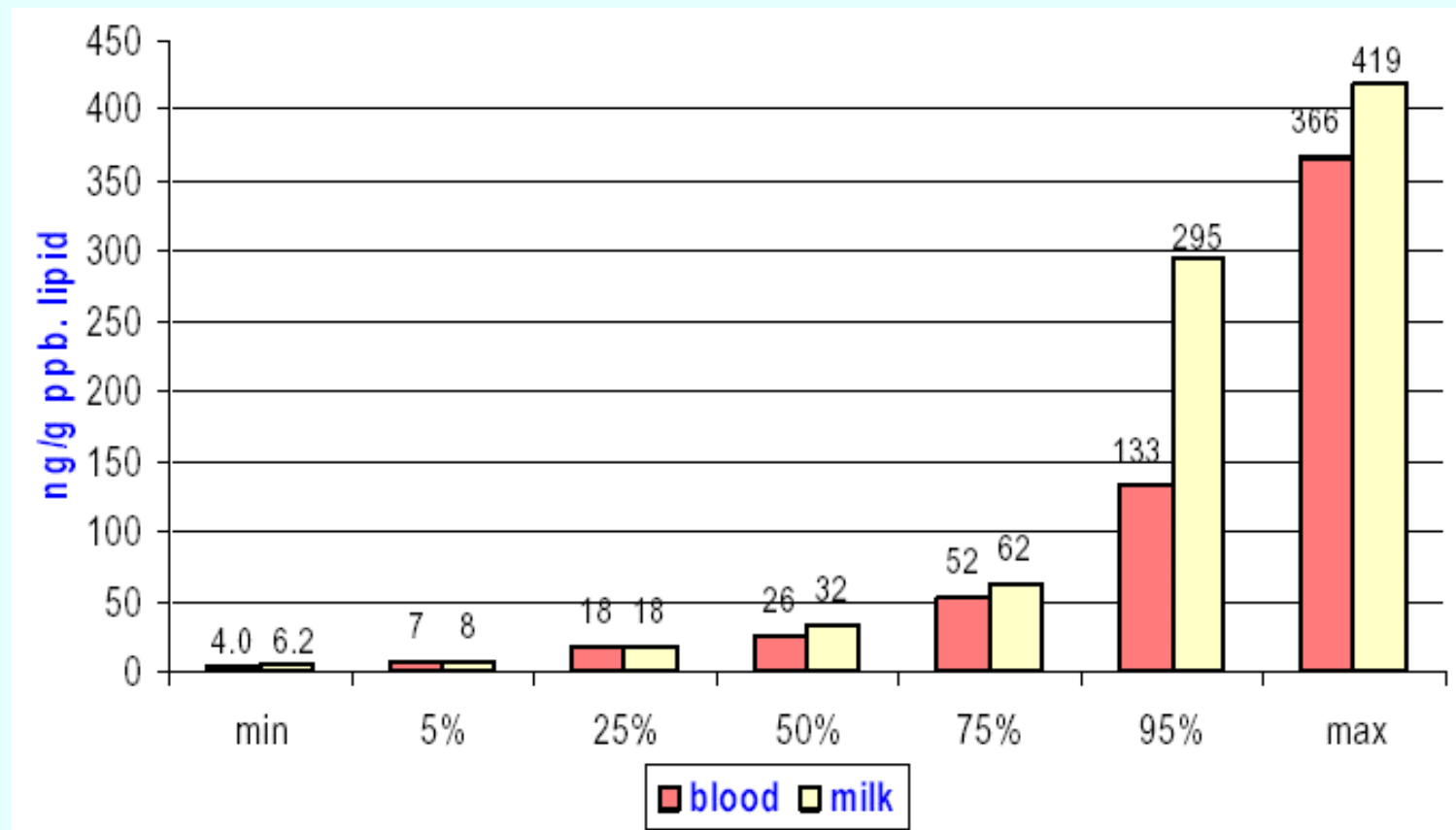
One-third have higher levels of PBDEs compared to PCBs



She *et al.*, 2005

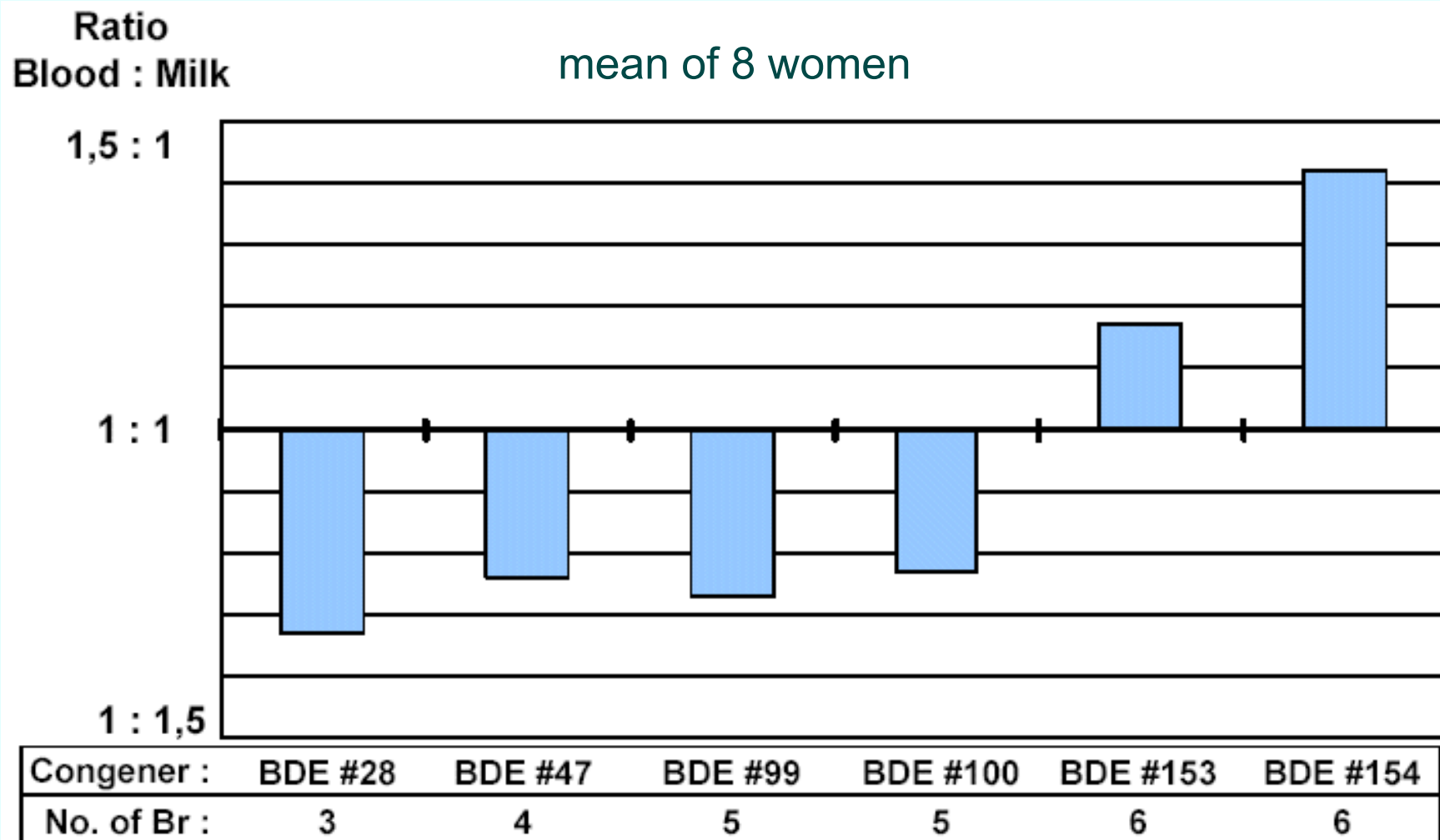
Population-Based PBDE Levels in U.S. Human Blood (n=50) and Milk (n=62), 2005

- 13 congeners
- highest levels reported worldwide



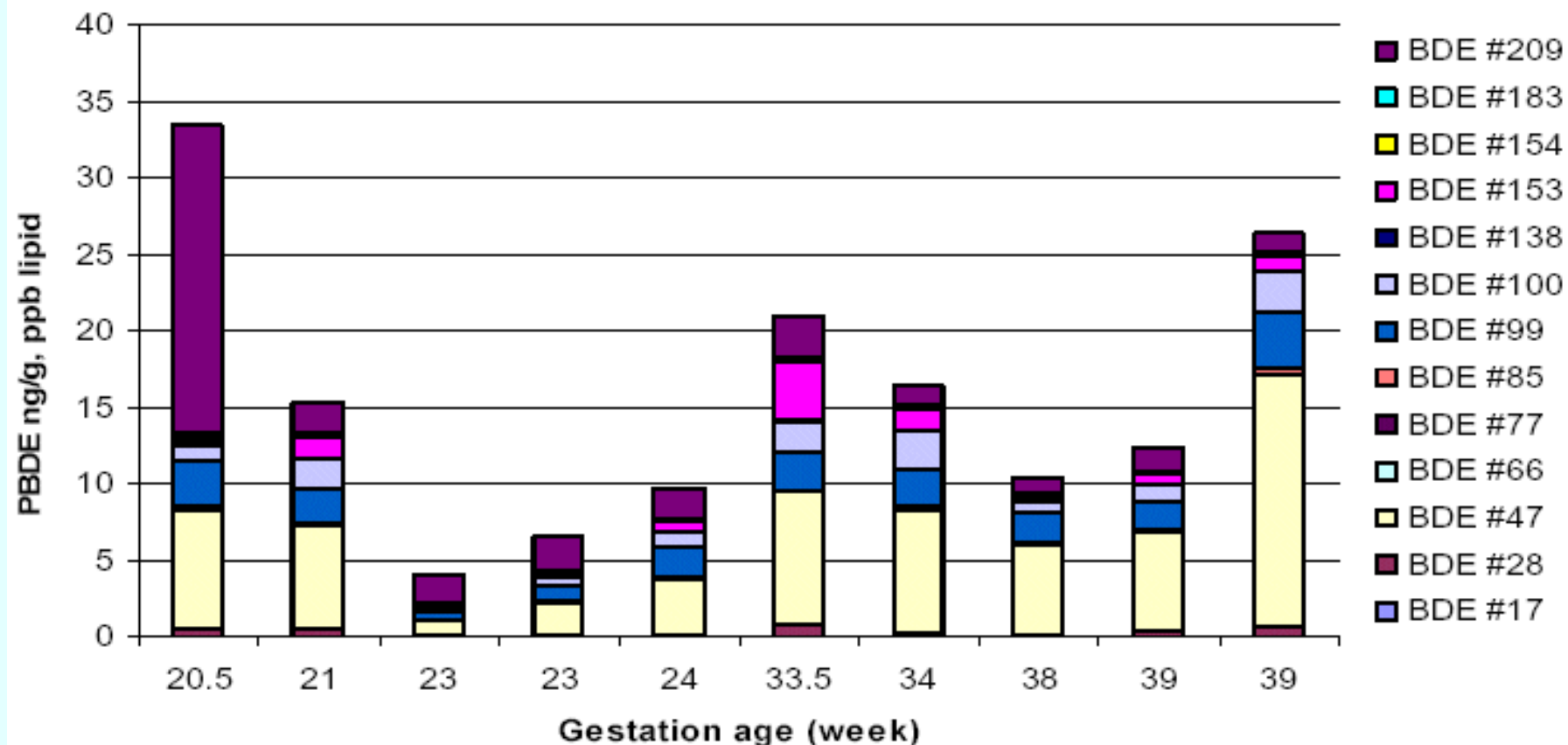
Schechter *et al.*

PBDE Partitioning Between Human Blood and Milk



Schechter *et al.*

PBDE Levels in Fetal Liver in Humans



	Minimum	Median	Mean	Max
Human milk PBDEs (n=62)	6.2	31.9	66	419
Human blood PBDE (n=39)	4	30.5	57	365
Fetal liver (n=10)	4	13.8	15.5	33.4

Schechter *et al.*

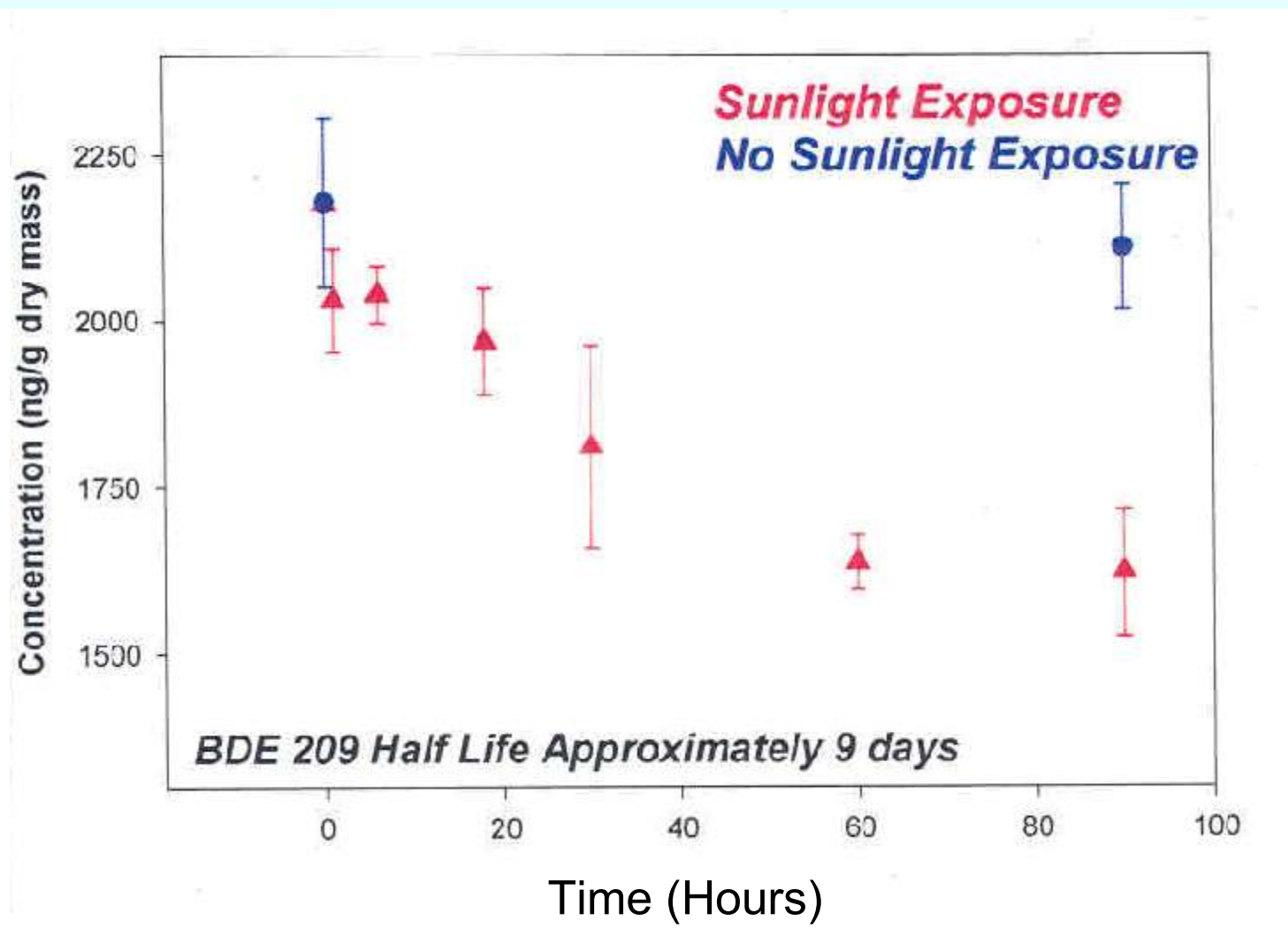
Behavior of decaBDE in the Environment

- ◆ Undergoes long-range transport, including into the Arctic (levels of PBDEs highest near cities)
- ◆ Levels of PBDEs in sediment have increased by several orders of magnitude since the 1970s
 - deca is dominant congener, >90% in many cases
- ◆ High levels in sewage sludge, deca dominant
 - one-half of sludge used as fertilizer
- ◆ High levels near waste dumps, dibenzofurans produced during burning

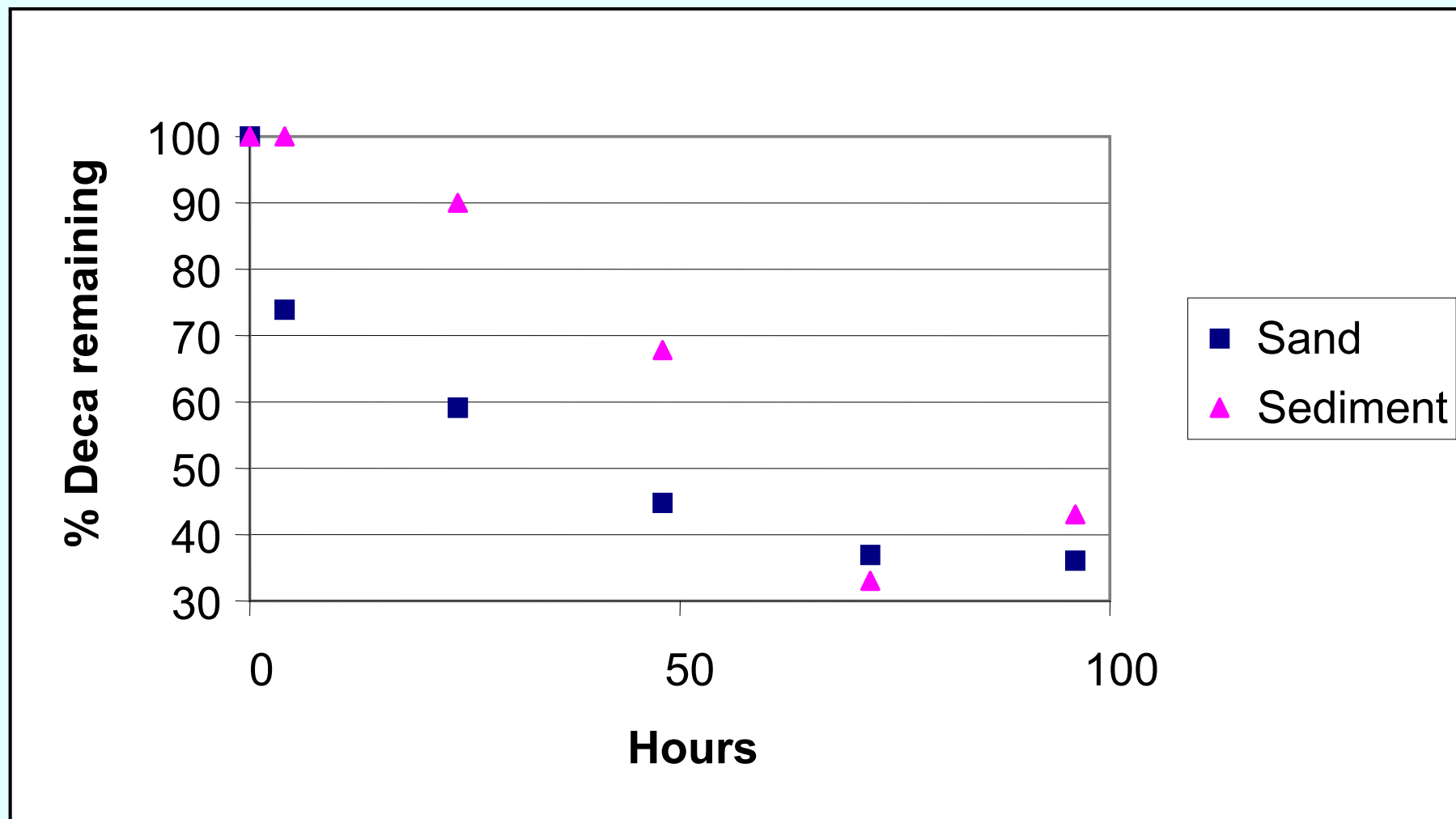
Behavior of decaBDE in the Environment

- ◆ Undergoes relatively rapid photodegradation, nona- and octa- congeners, 153, 154, 183
- ◆ Degraded by microorganisms in sediment
 - products may include 47, 99, 100, 153, -OH and methoxy metabolites
 - suggests contribution of deca BDE is underestimated

Debromination of DecaBDE in Dust Exposed to Sunlight

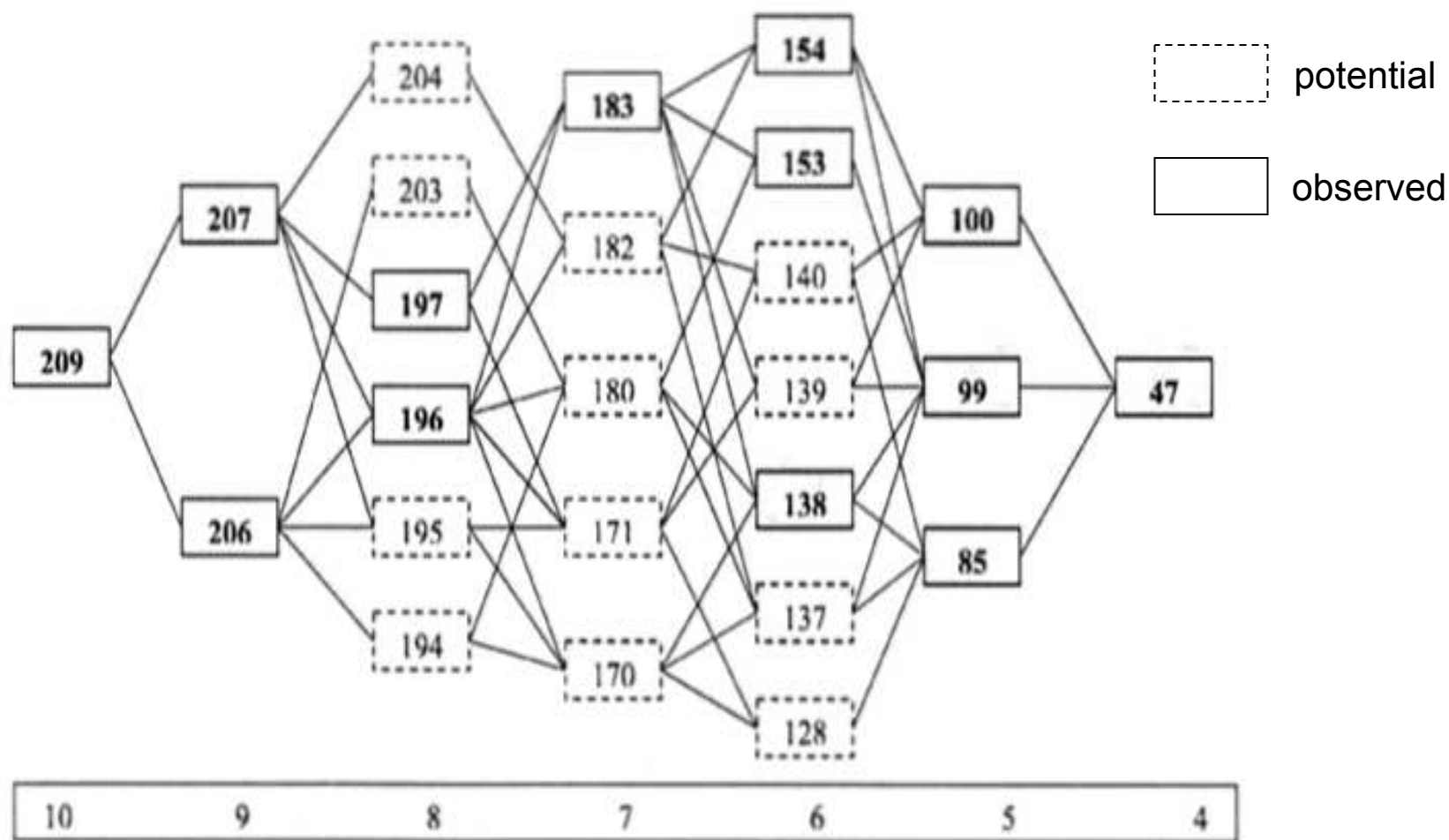


Debromination of DecaBDE in Sand or Sediment Exposed to Sunlight



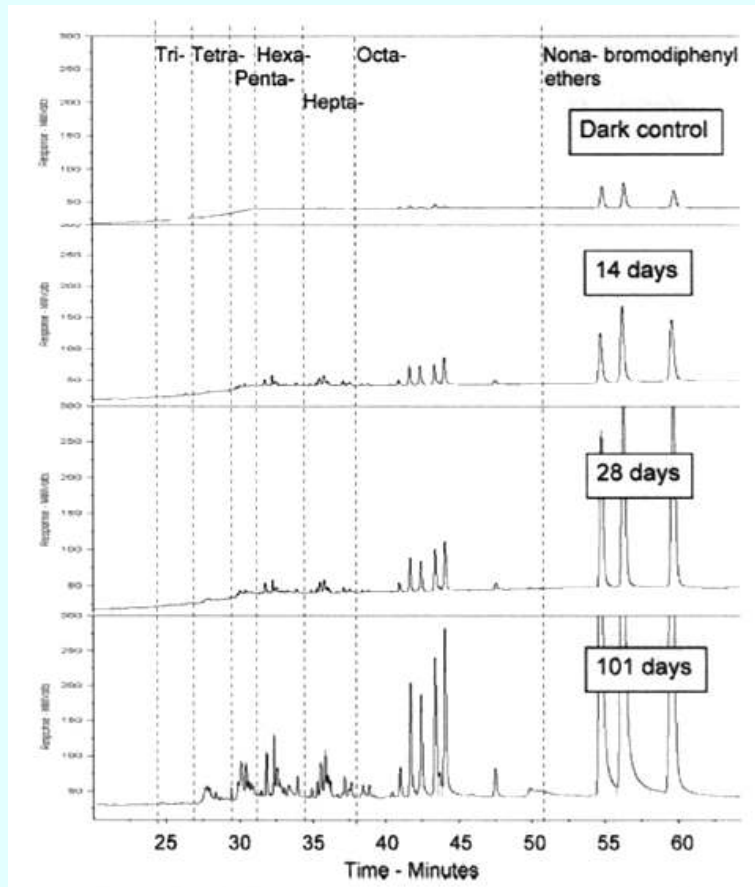
Söderström *et al.*, 2004

Intermediates in Photopic Debromination of decaDBE in Hexane to BDE47

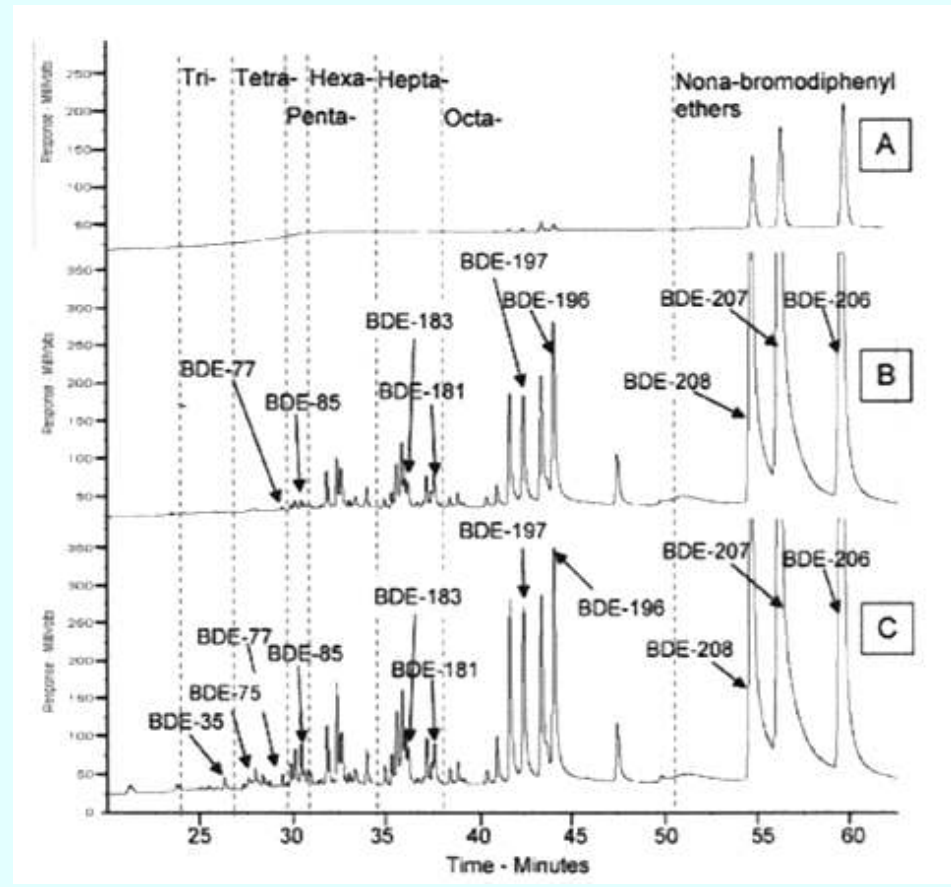


Cruz *et al.*, Environ. Sci. Technol., 2004

Photodegradation of DecaBDE By Sunlight



GC-ECD chromatograms showing appearance of PBDE congeners after sunlight irradiation of BDE-209



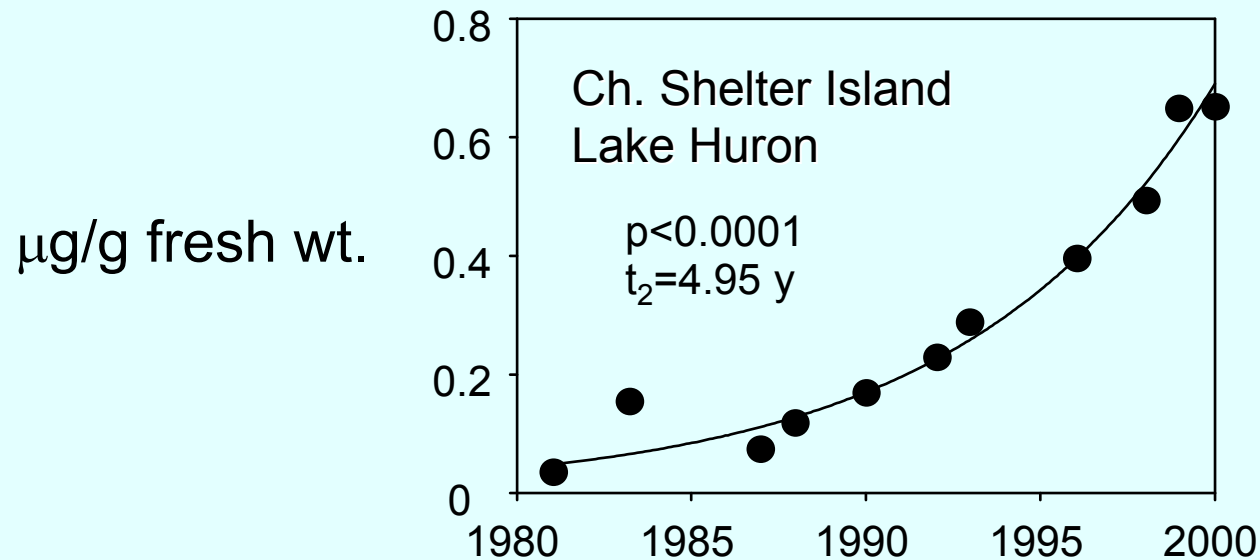
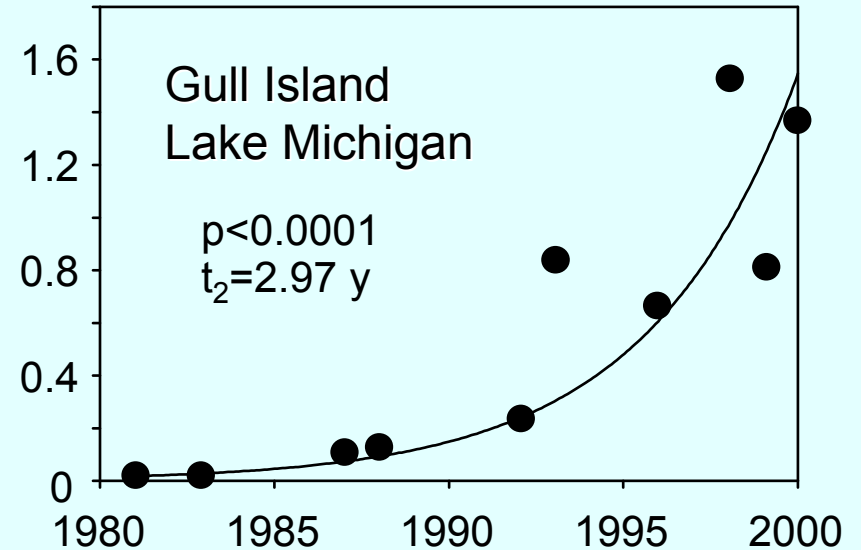
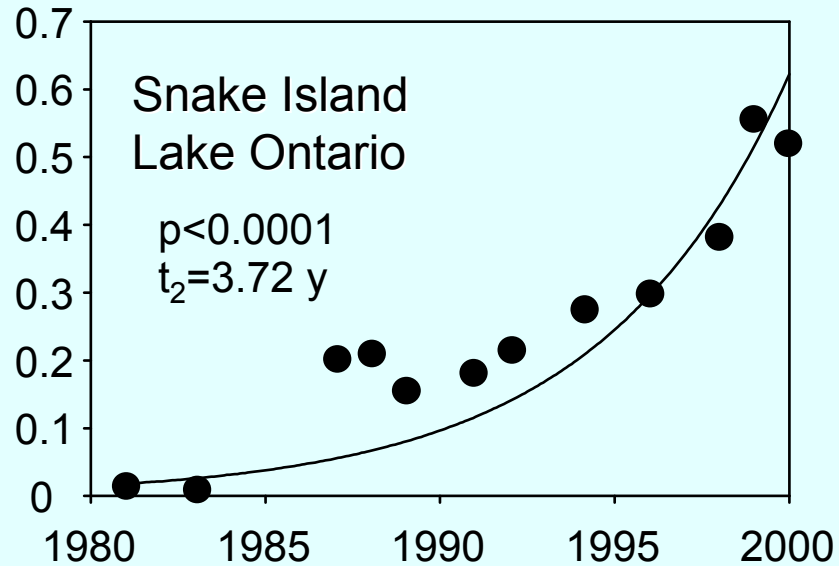
GC-ECD chromatograms of concentrated dark control (A) and sunlight-irradiated kaolinit (b) and montmorillonite (C) at 56 days

Ahn *et al.*, Environ. Sci. Technol., 2006

Behavior of PBDEs in Animals

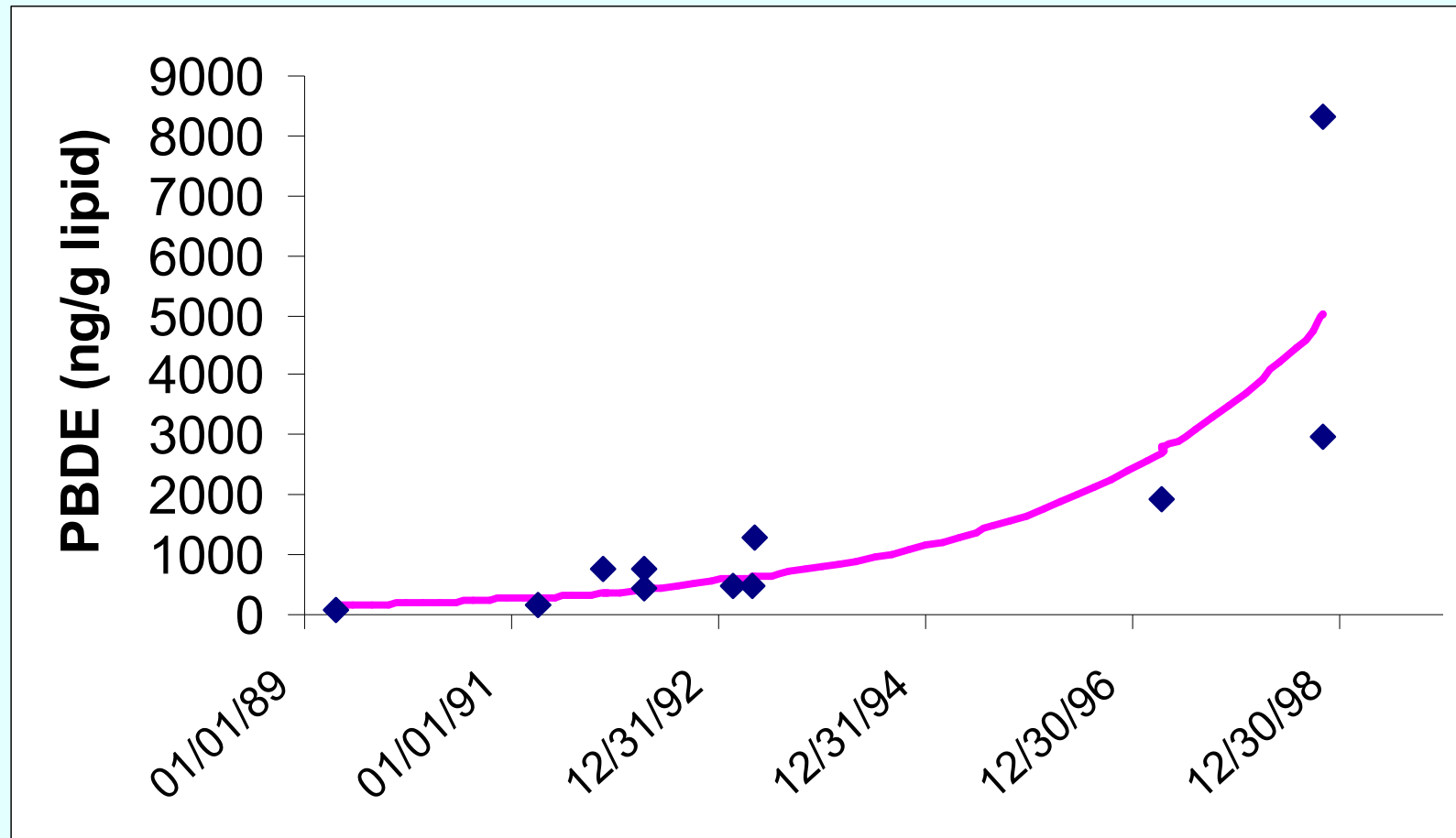
- ◆ Levels in wildlife are increasing exponentially around the world
- ◆ Found in fish in remote mountain lakes, Arctic mammals
- ◆ Animals and birds at the top of the food chain particularly affected
 - predatory fish, terrestrial and aquatic predatory birds (numerous species), herring gulls, whales, harbor seals

PBDEs in Herring Gull Eggs - Great Lakes



Alaee, 2002

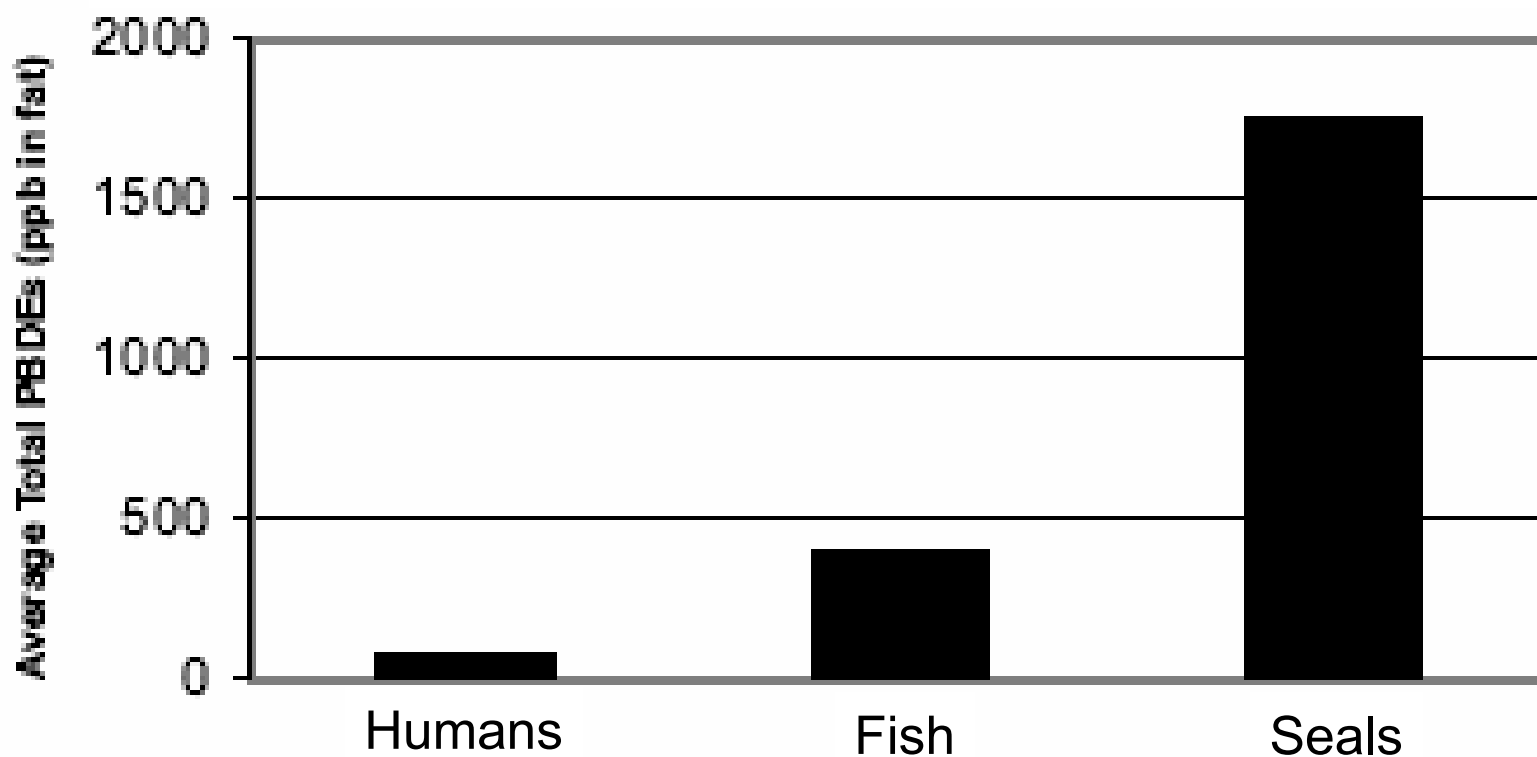
PBDEs in Blubber of California Seals



N=11

She et al., 2002

Levels of PBDEs in San Francisco Bay Area Late 1990s

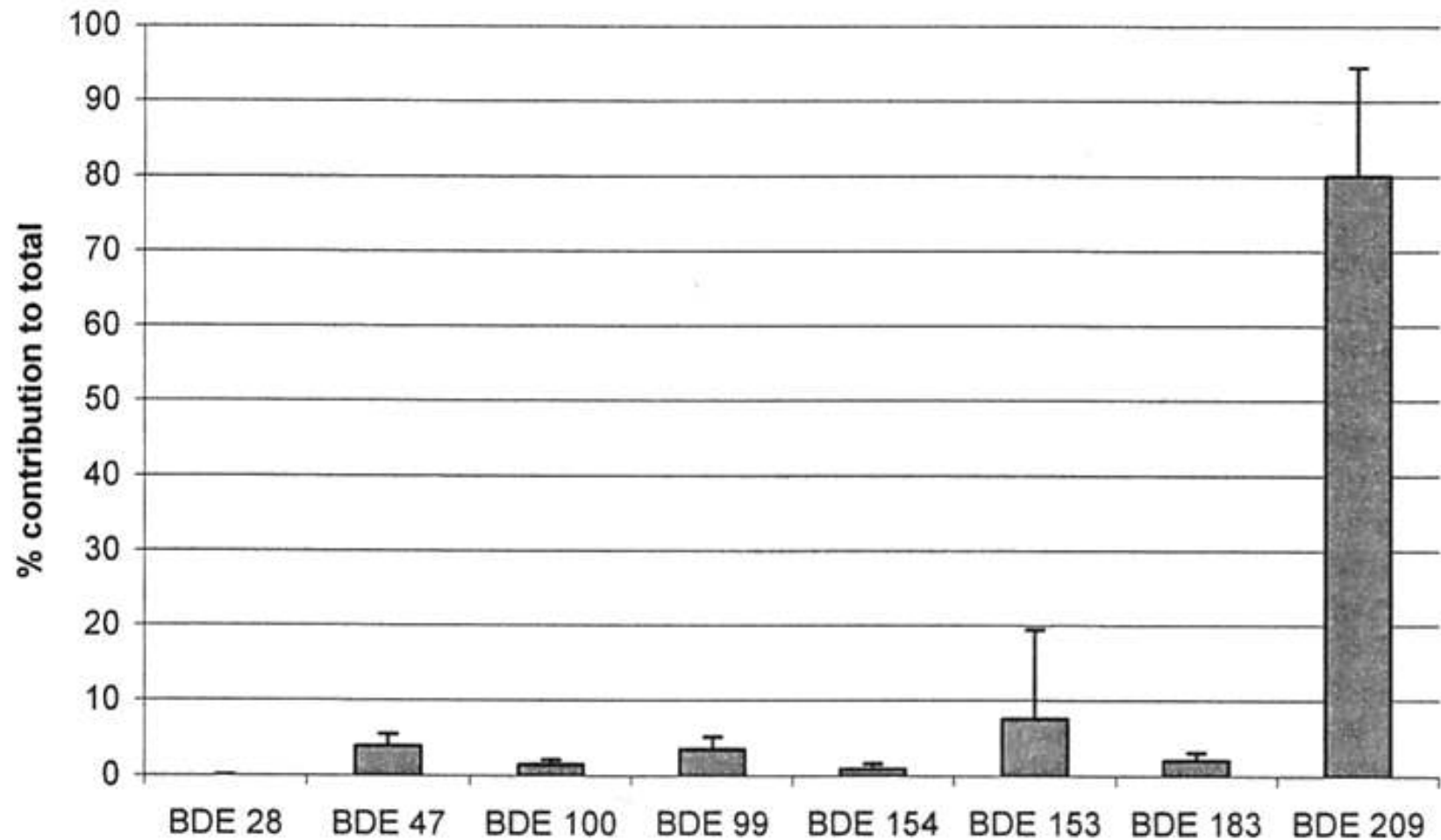


She et al.

Behavior of deca BDE in Animals

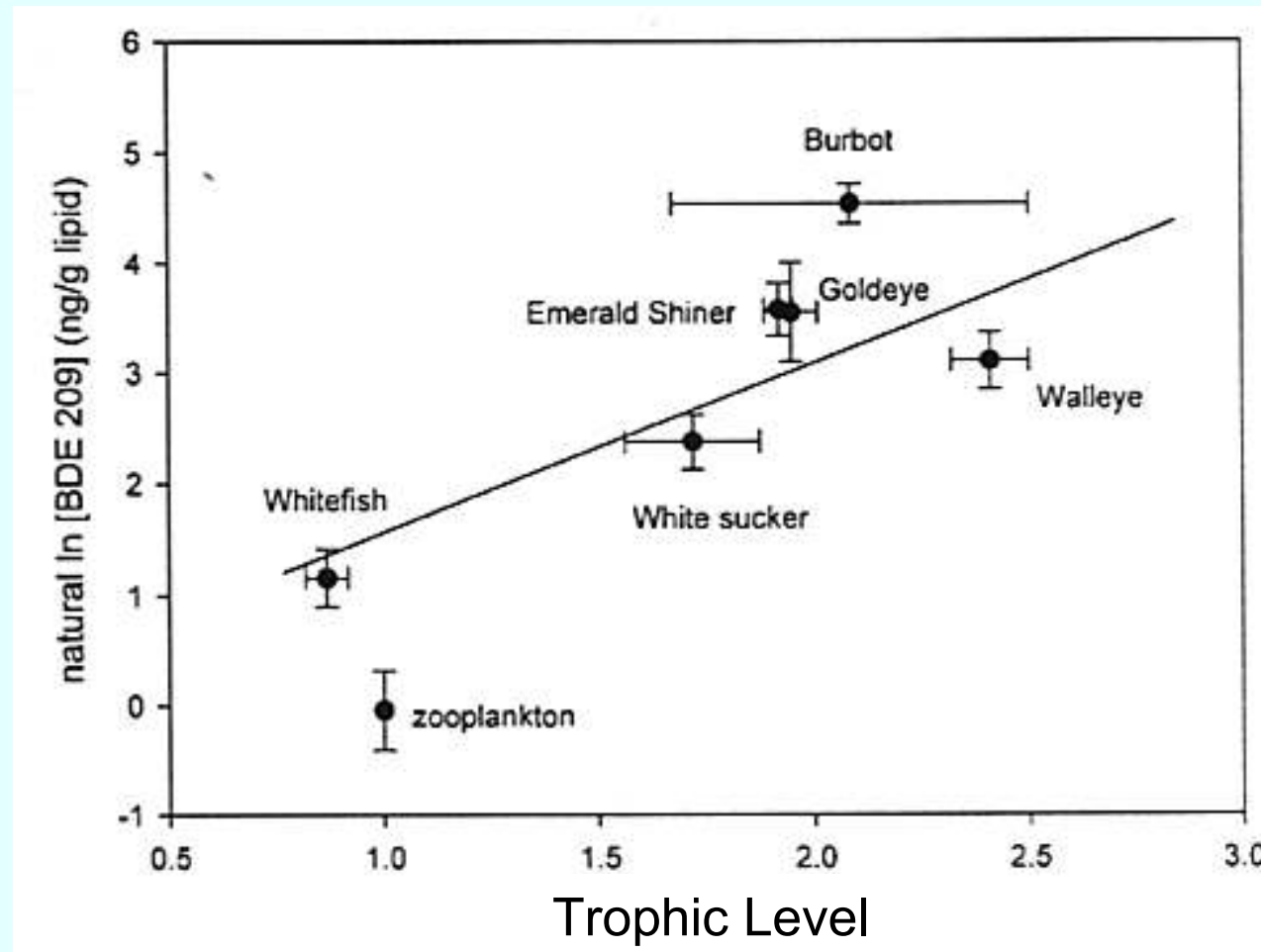
- ◆ Found in top predators in aquatic, terrestrial and aquatic food webs
 - concentrations often but not always low compared to other congeners
- ◆ Degradation and metabolism may result in underestimation of contribution of deca

Median PBDE Profile in Red Fox



Voorspoels *et al.*, Environ. Sci. Technol., 2006

Concentration of DecaBDE by Trophic Level Lake Winnipeg, Canada

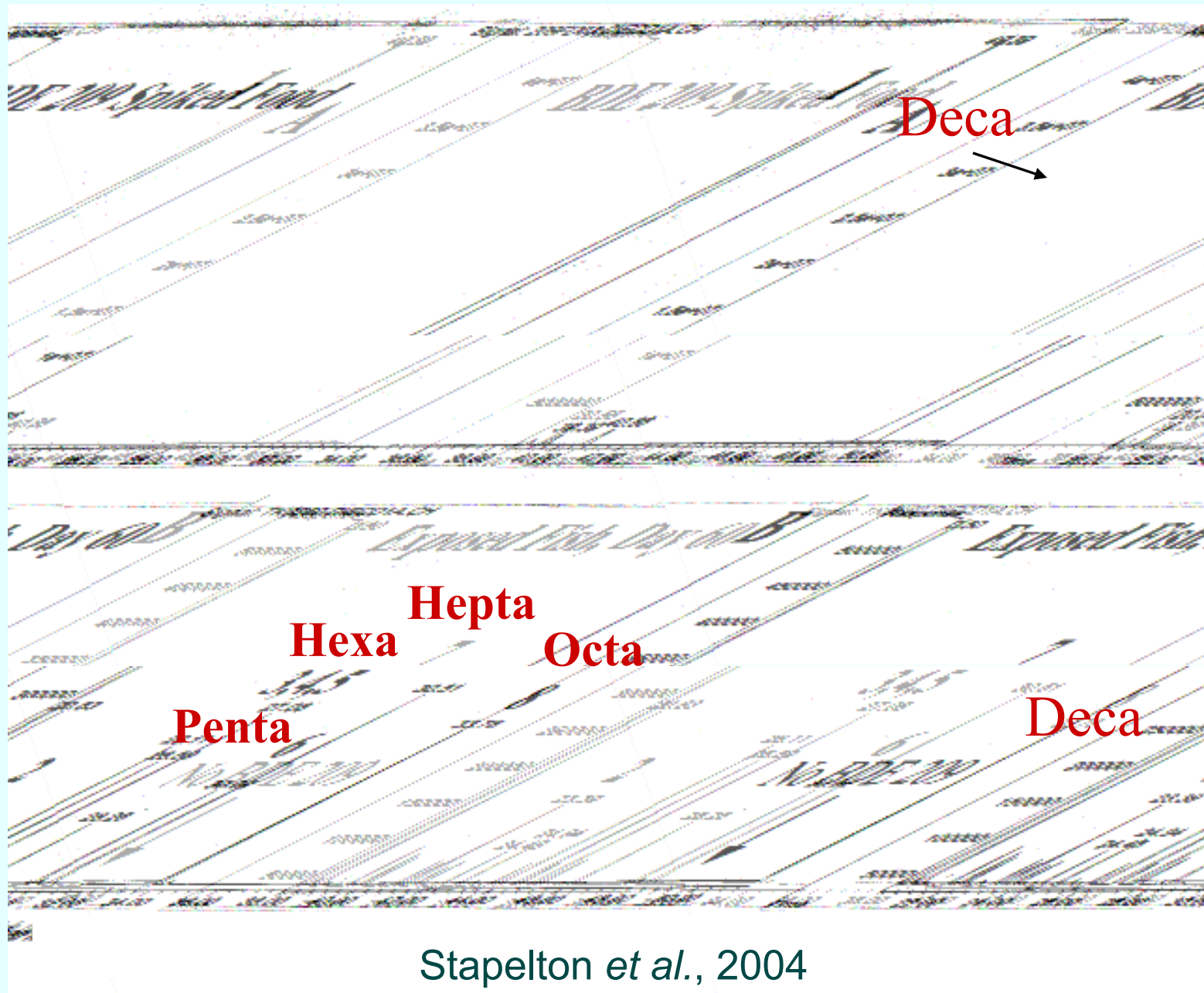


Law *et al.*, Environ. Toxicol. Chem., 2006

Metabolism of decaBDE

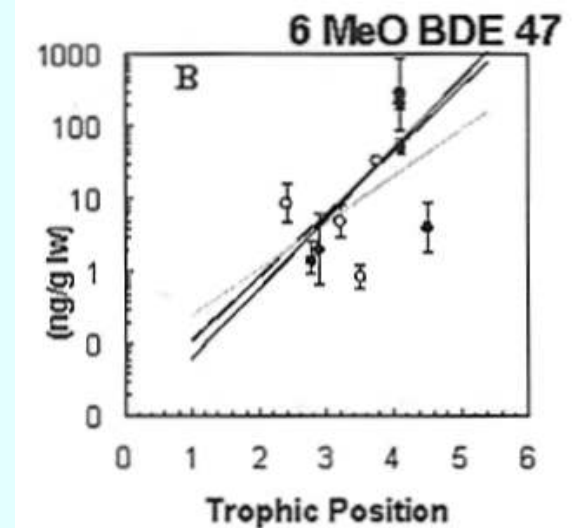
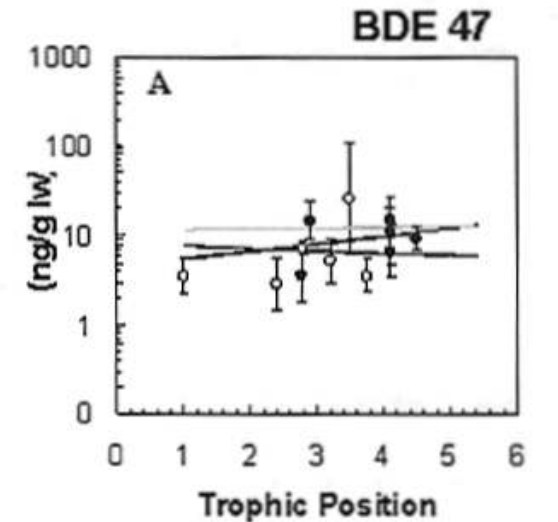
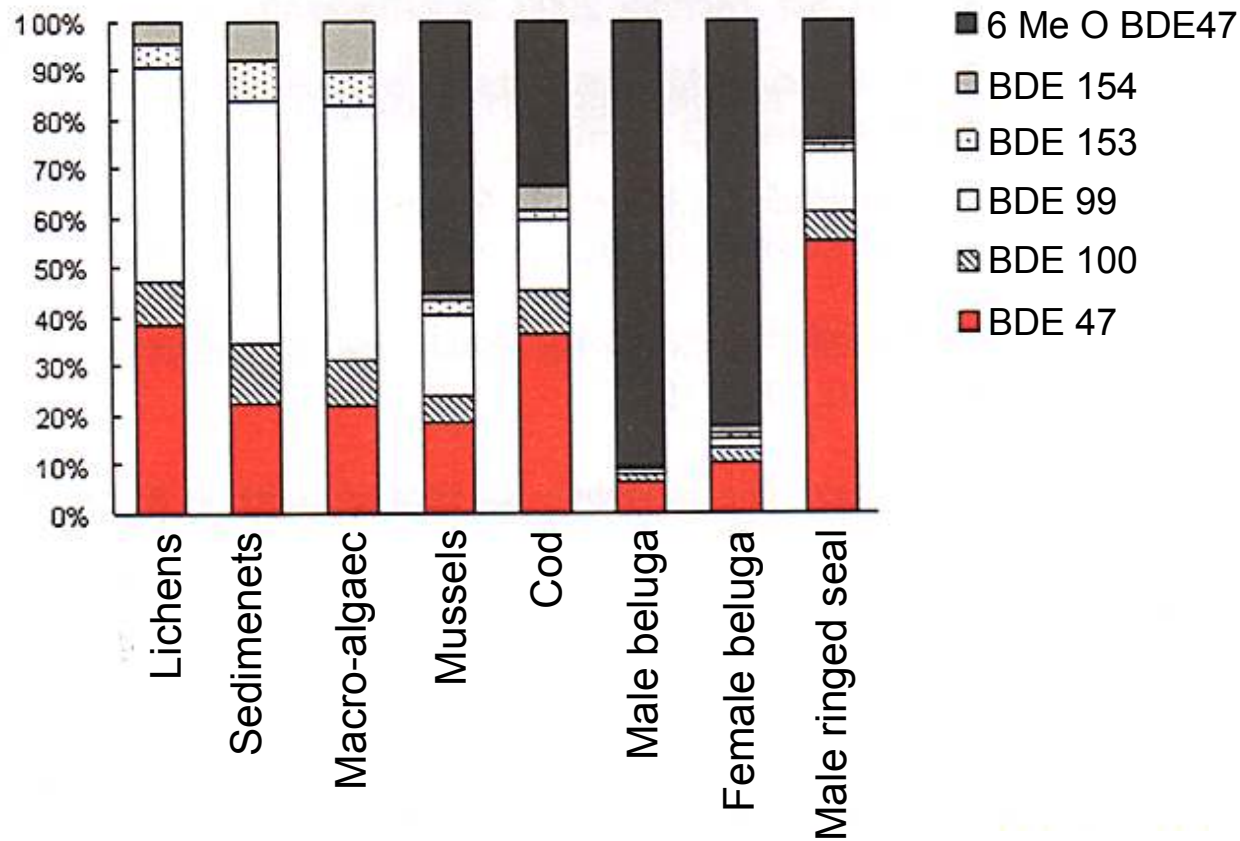
- ◆ decaBDE is absorbed, as much as >60% in some studies
- ◆ decaBDE metabolized by fish and mammals to nona, octa, hexa, and penta BDEs, including 153, 154, 183, 203, 206
- ◆ Hydroxy- and methoxy- metabolites identified in experimental studies, wild animals and humans
- ◆ decaBDE or metabolites gets into brain
- ◆ Mice pups do not excrete PBDEs after single dose of BDE-47

Metabolism of DecaBDE By Carp



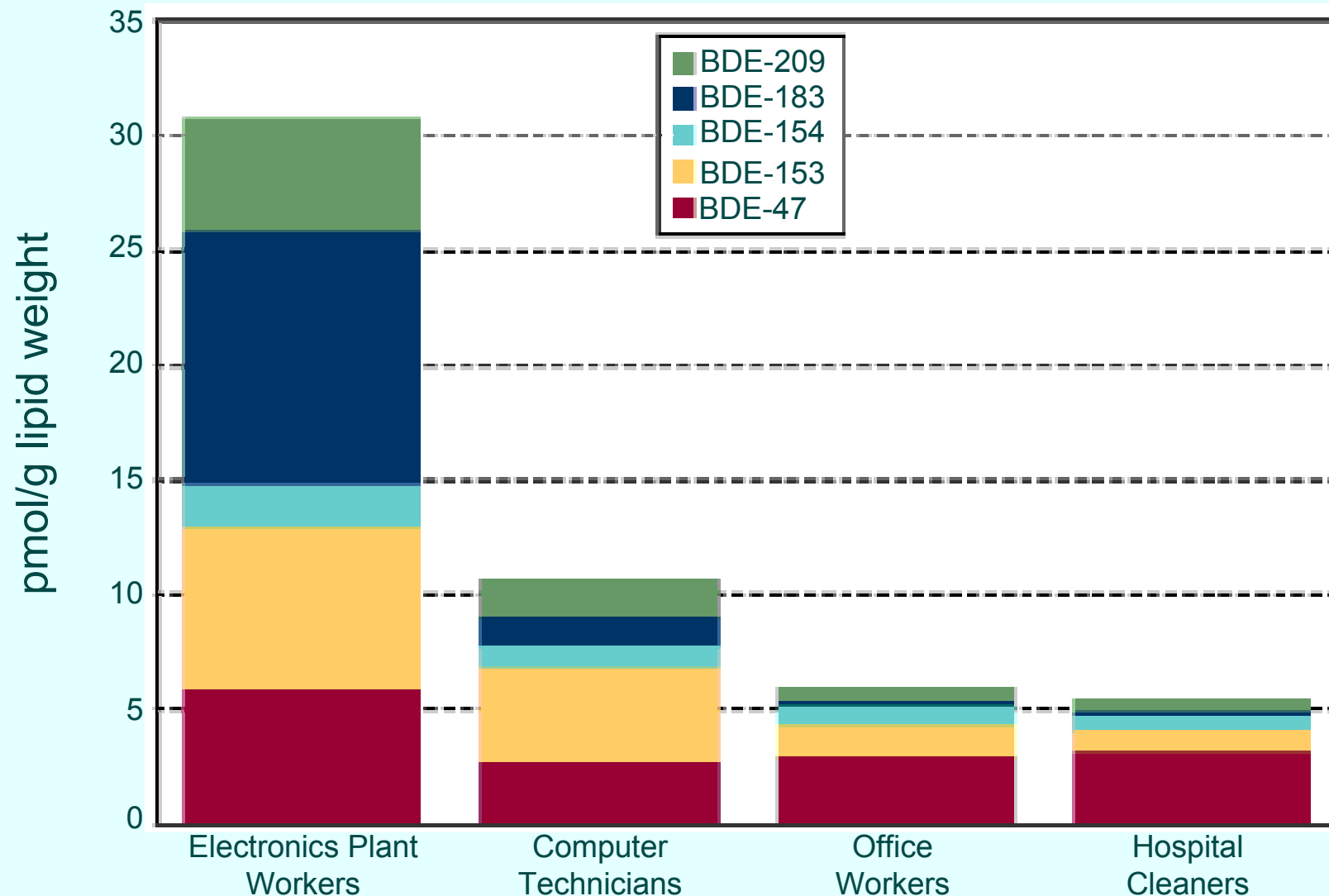
Stapelton *et al.*, 2004

Bioconcentration of BDE-47 Metabolite



Kelly and Ikonomou, 2006

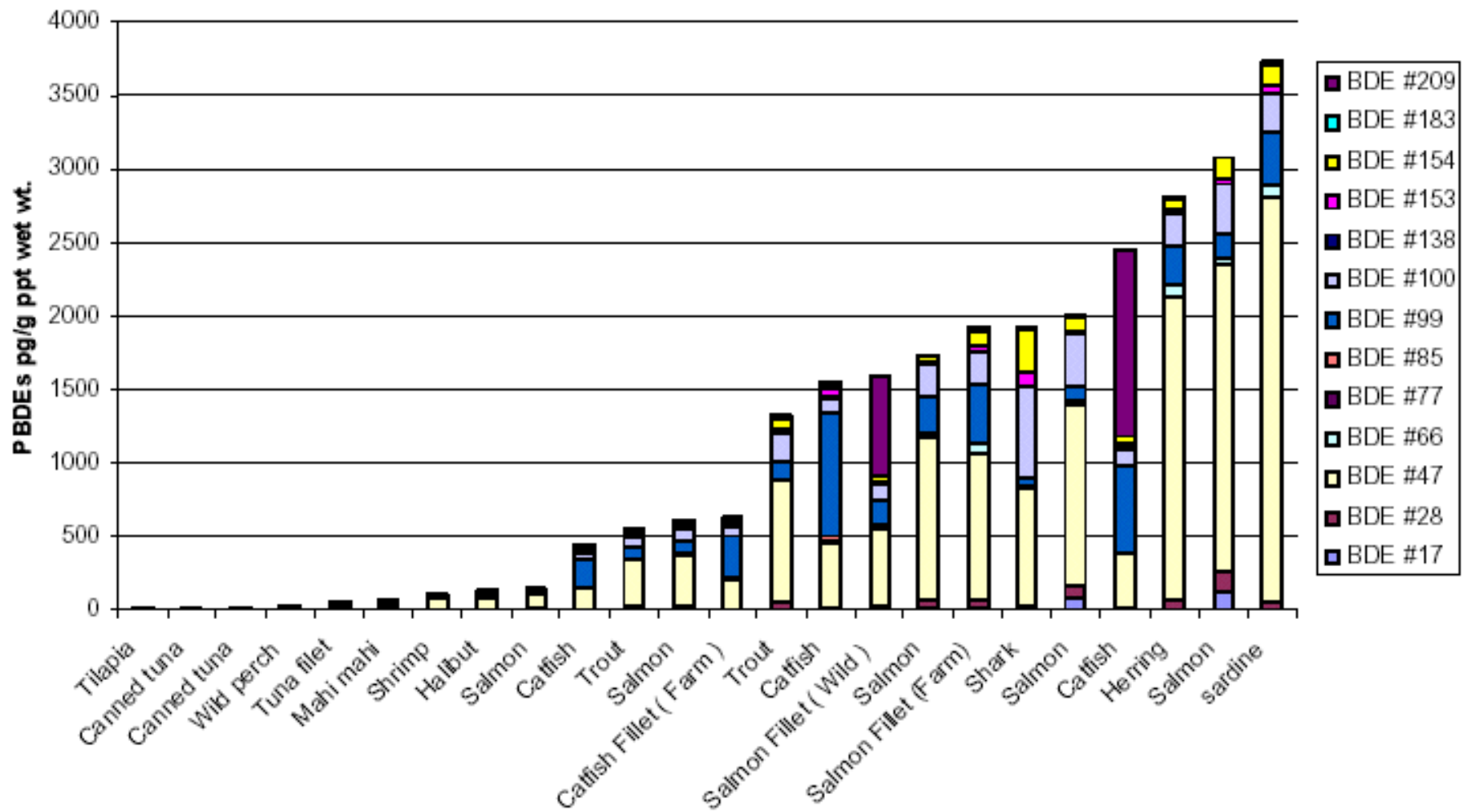
Concentration of Five Most Abundant PBDEs in Swedish Workers' Blood



Thuresson *et al.*, 2005

Sources of PBDE Exposure in Humans

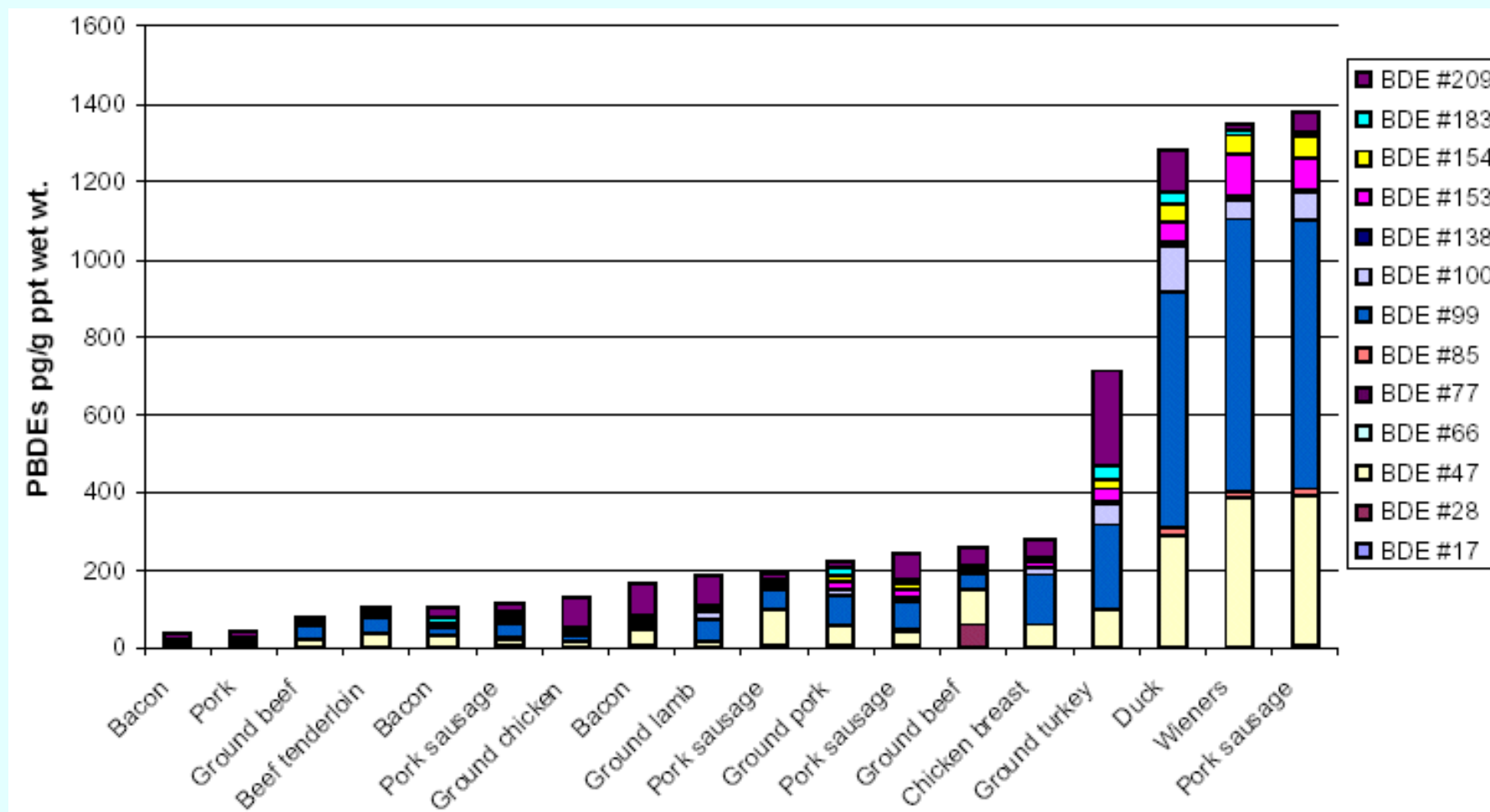
PBDE Congener Levels in Fish in the U.S.



fish n=24; range: 11-3726 pg/g; mean: 1120 pg/g; median: 616 pg/g

Schechter *et al.*

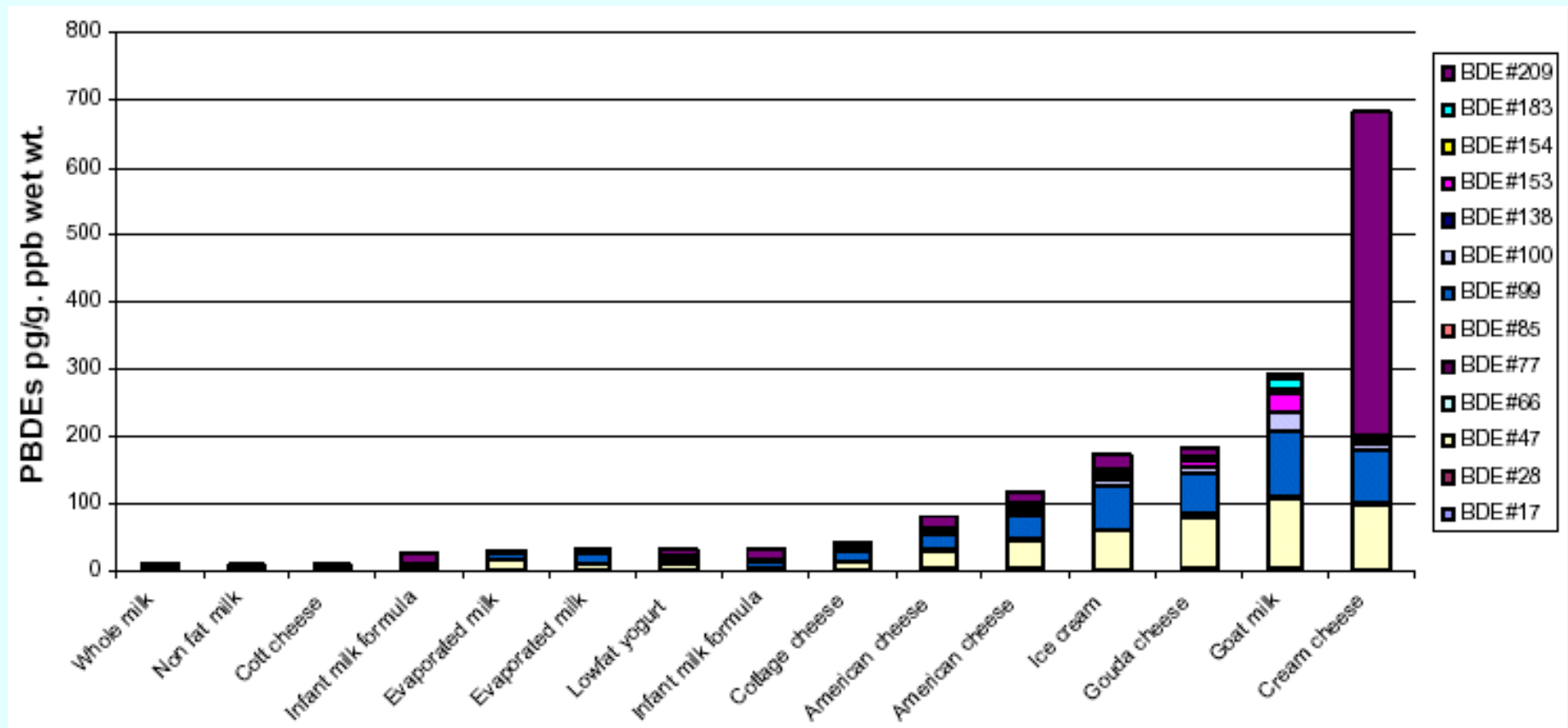
PBDE Congener Levels of Meat in the U.S.



meat n=18; range: 39-1378 pg/g; mean: 383 pg/g; median: 190 pg/g

Schechter *et al.*

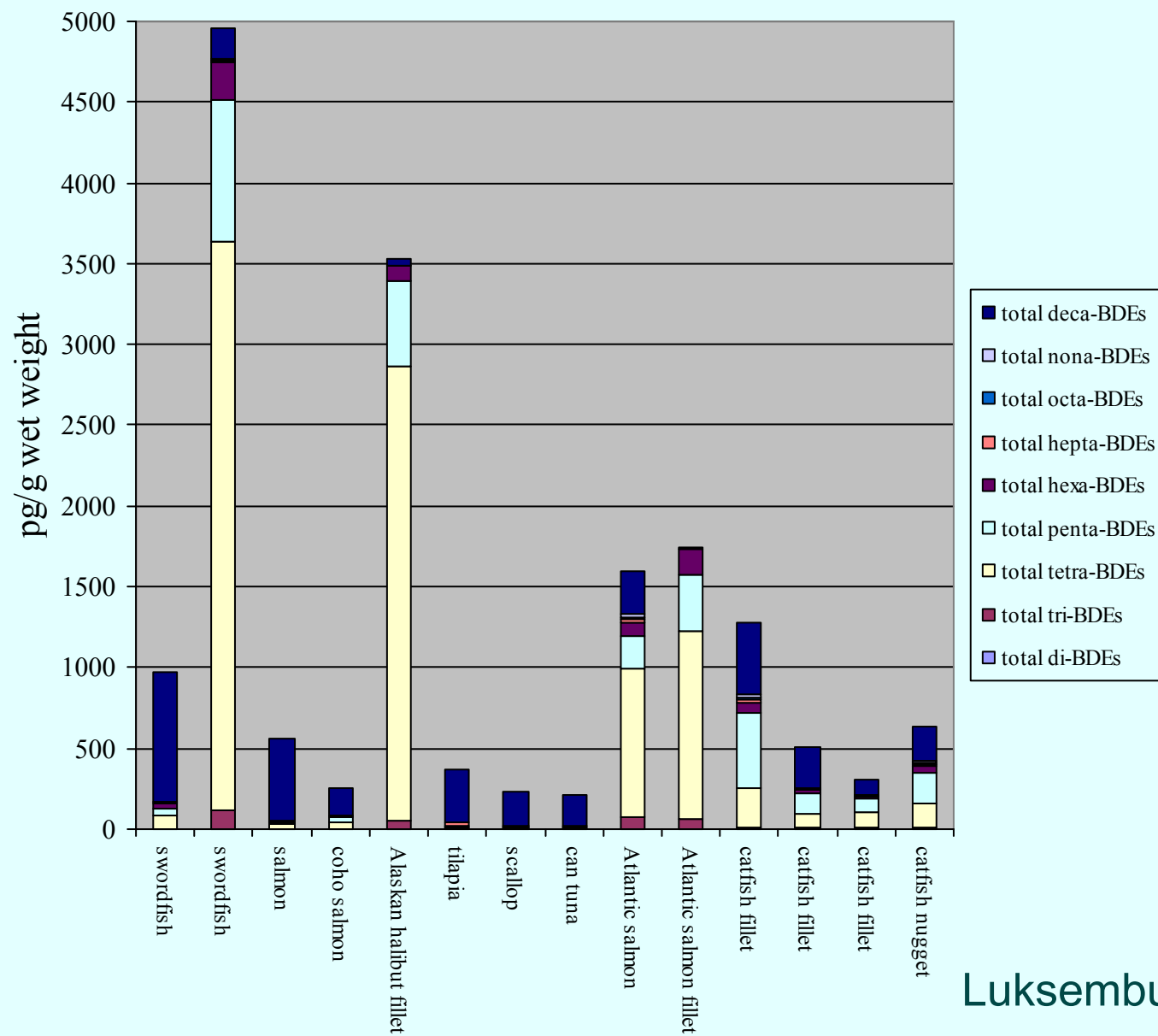
PBDE Congener Levels of Dairy Products in the U.S.



dairy n=15; range: 7.9-683 pg/g; mean: 116 pg/g; median: 32.2 pg/g

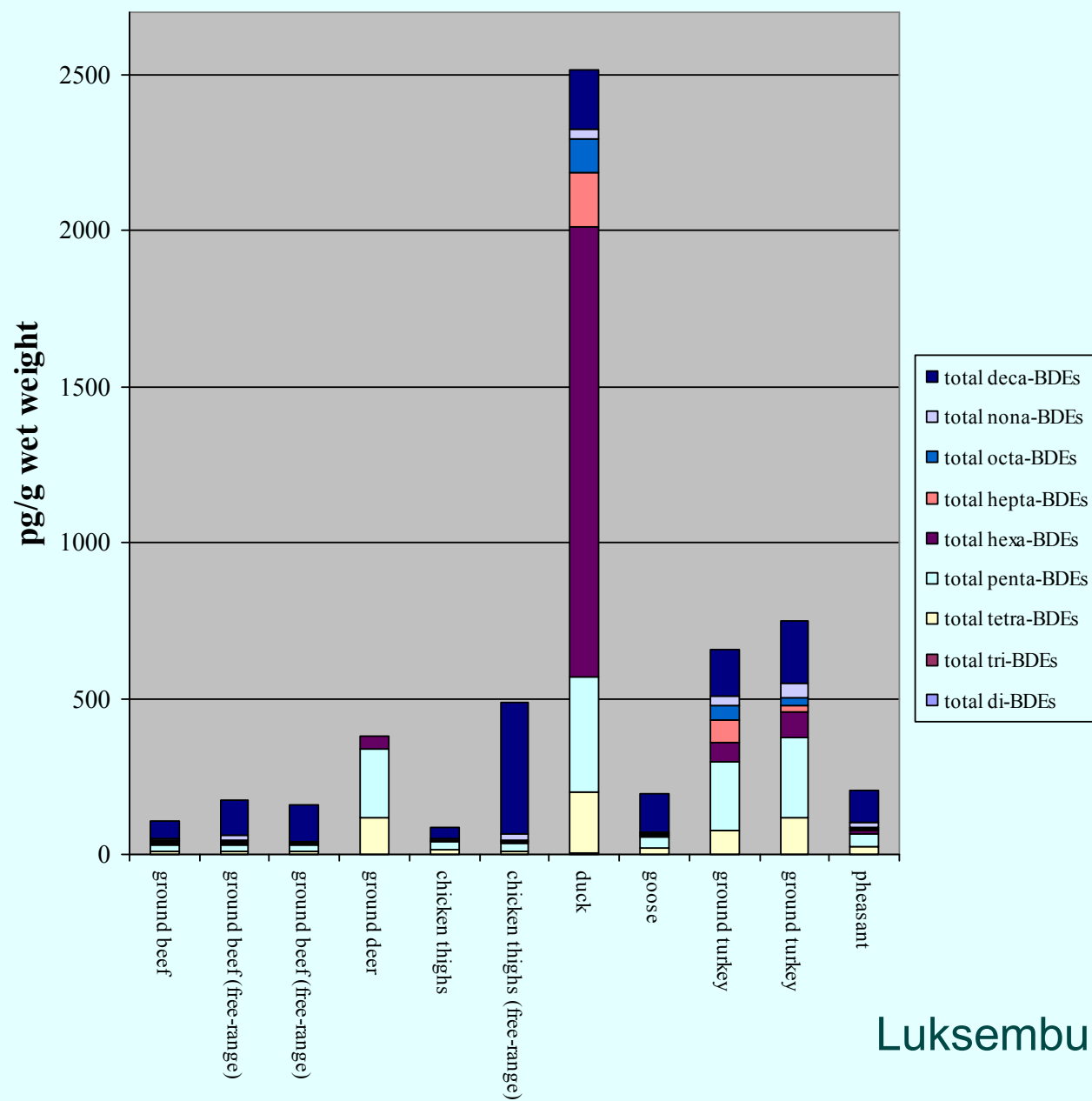
Schechter *et al.*

PBDE Congener Levels in California Fish



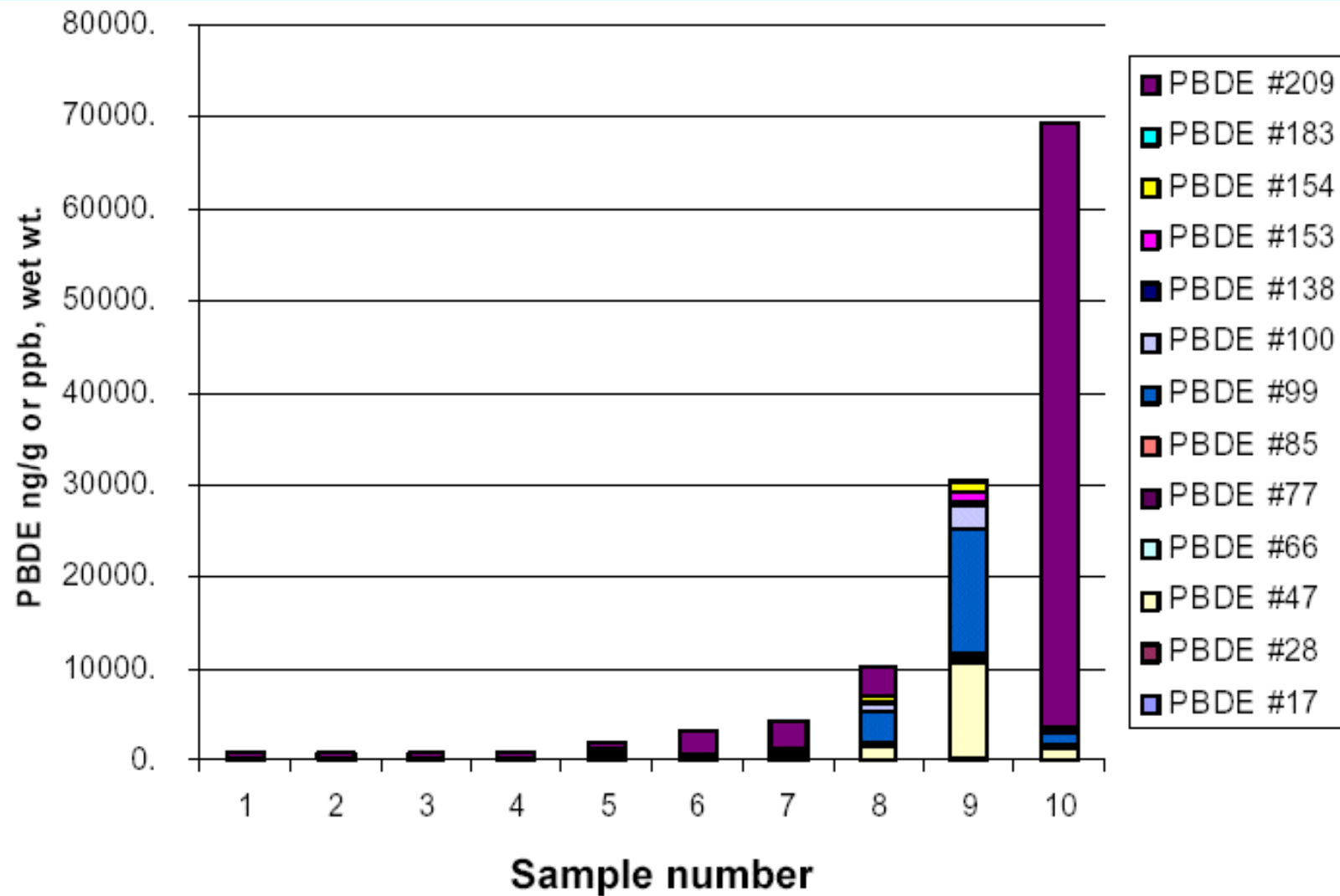
Luksemburg et al., 2004

PBDE Congener Levels in California Meat and Poultry



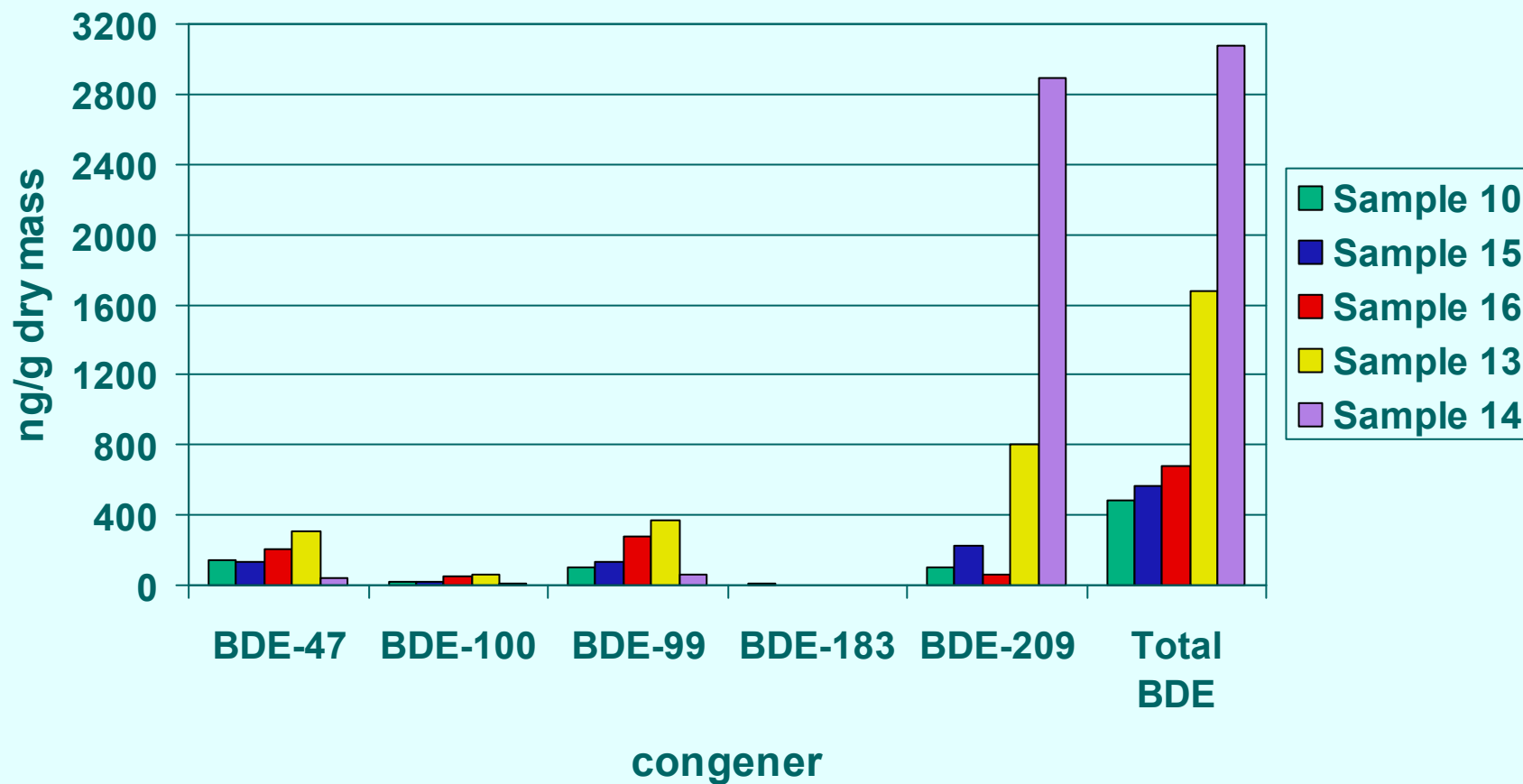
Luksemburg et al., 2004

PBDEs in U.S. Vacuum Sweeping



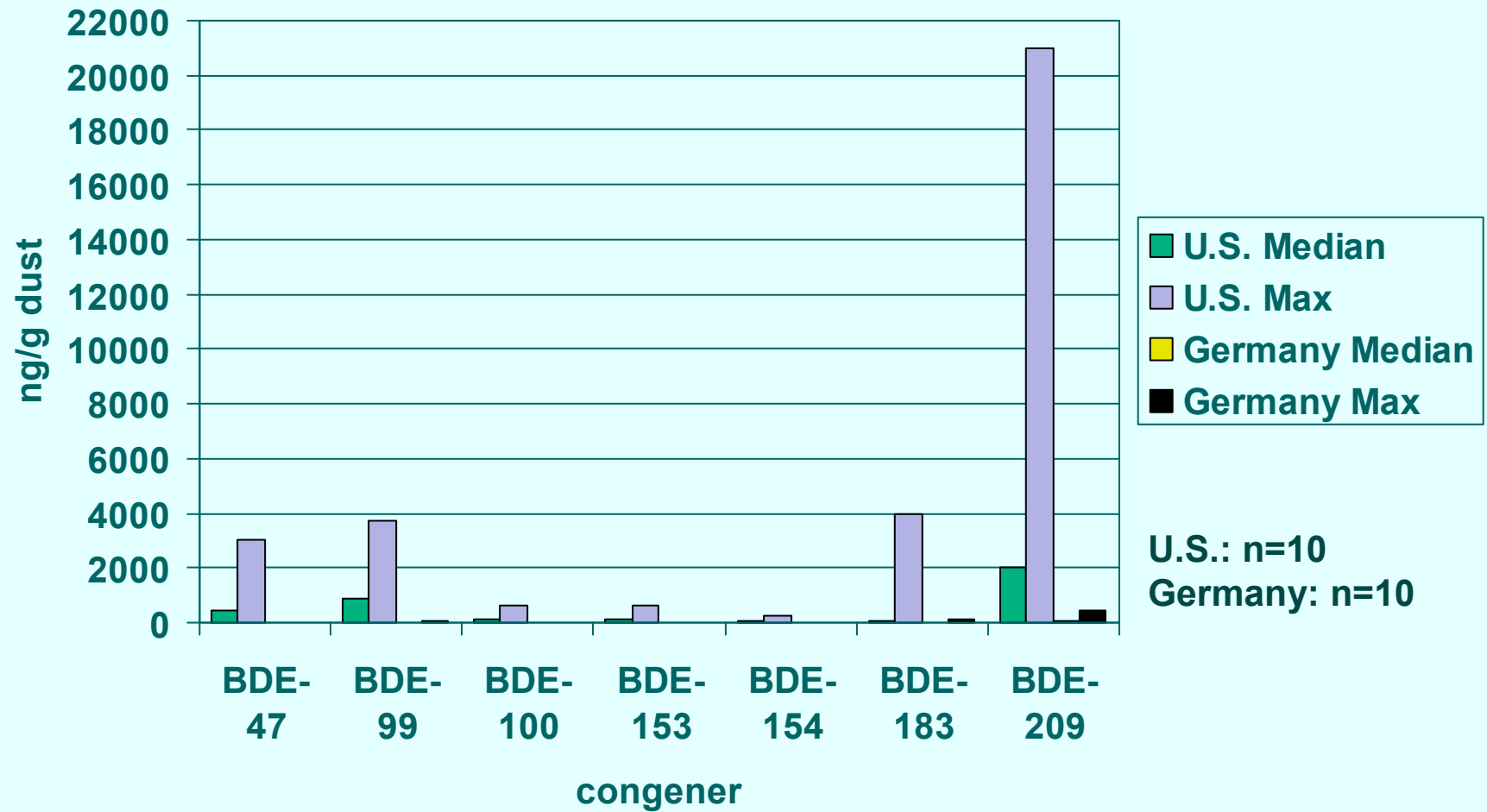
Schechter *et al.*

Concentrations of BDE Congeners in Home Dryer Lint



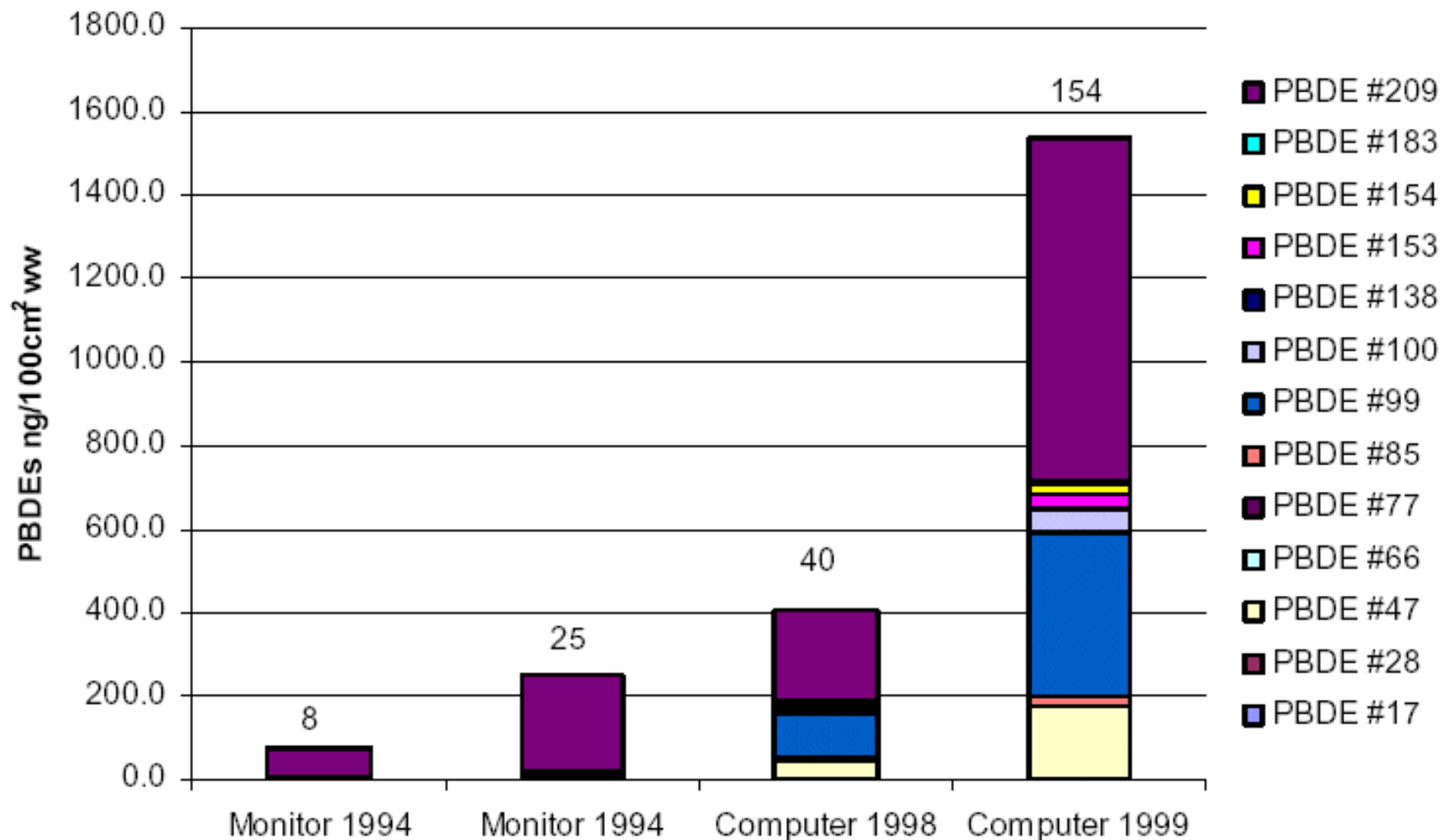
Stapleton *et al.*, 2005

Concentration of PBDEs in Dust



Sjodin *et al.*

PBDEs on Computer Surfaces



n=4, monitor range: 8-25 ng/100cm² ww, computer range: 40-154 ng/100cm² ww

Schechter *et al.*

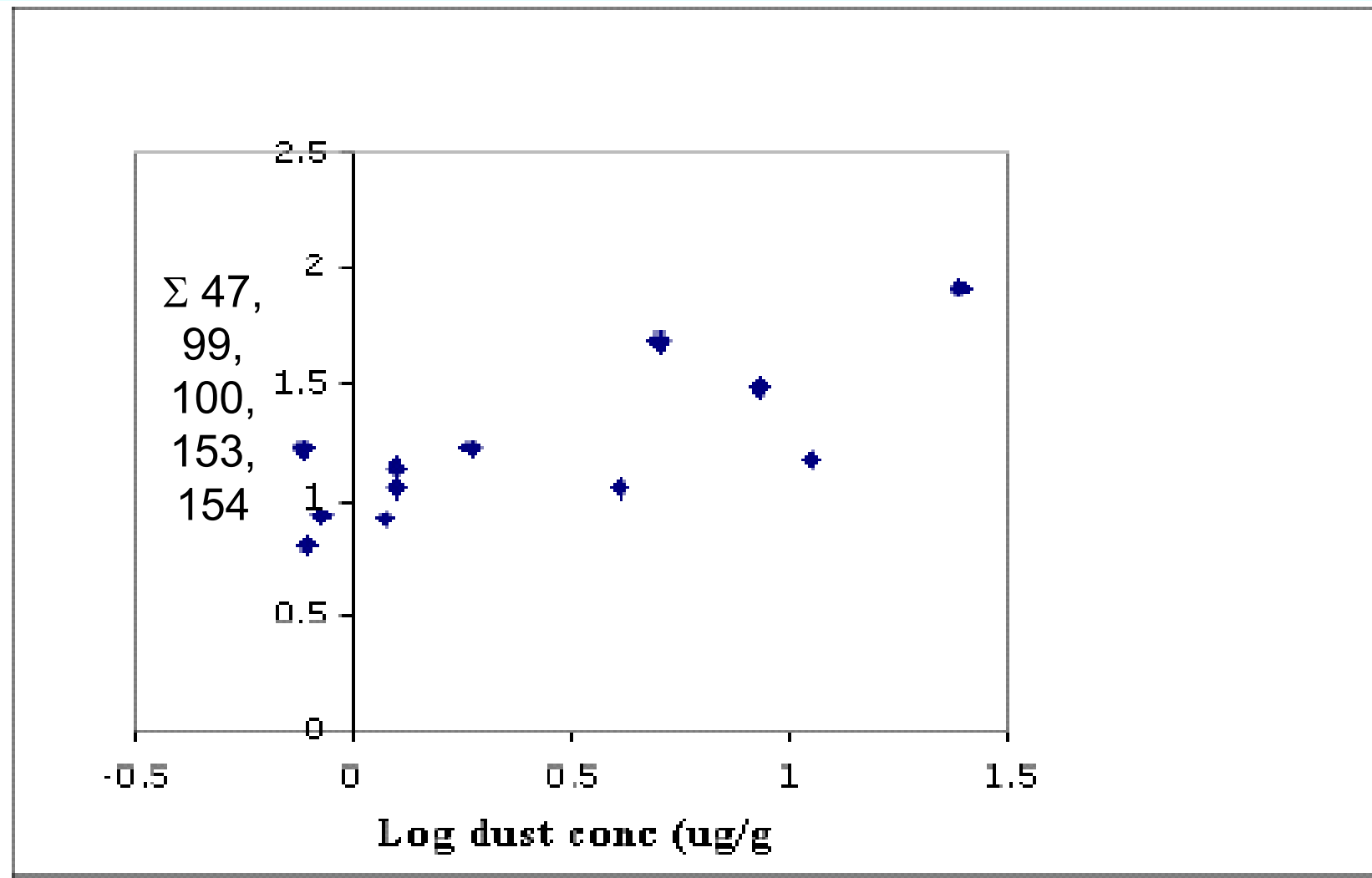
Brominated Flame Retardants in Dust on Computers

Maine samples (of 18 total) pg/cm²

	deca	octa	nona	TBBTA
state house	186	58	85	67
state house	11	5	12	0.02
children's museum	72	2	15	0.1

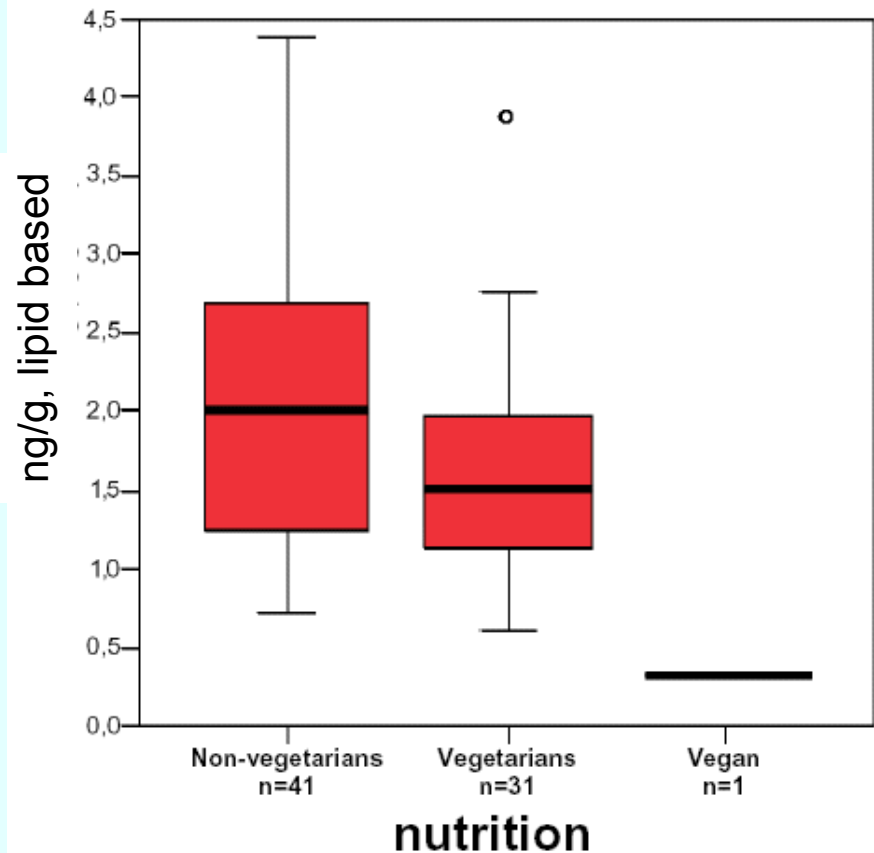
Computer Take-Back Campaign, 2004

Association Between Milk and House Dust PBDE Levels

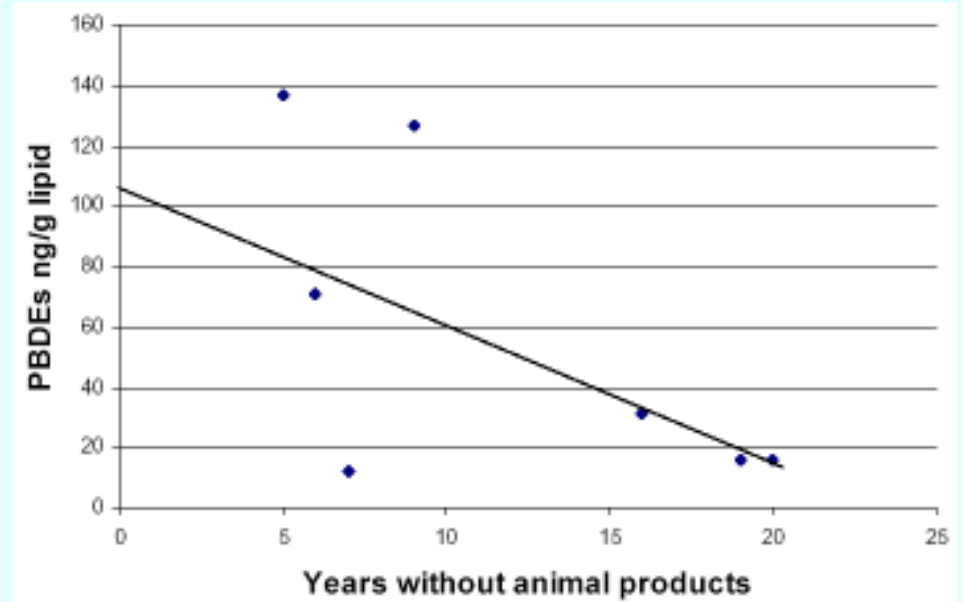


Wu *et al.*, 2005

Levels of PBDEs in Human Milk From Non-Vegetarians, Vegetarians and Vegans



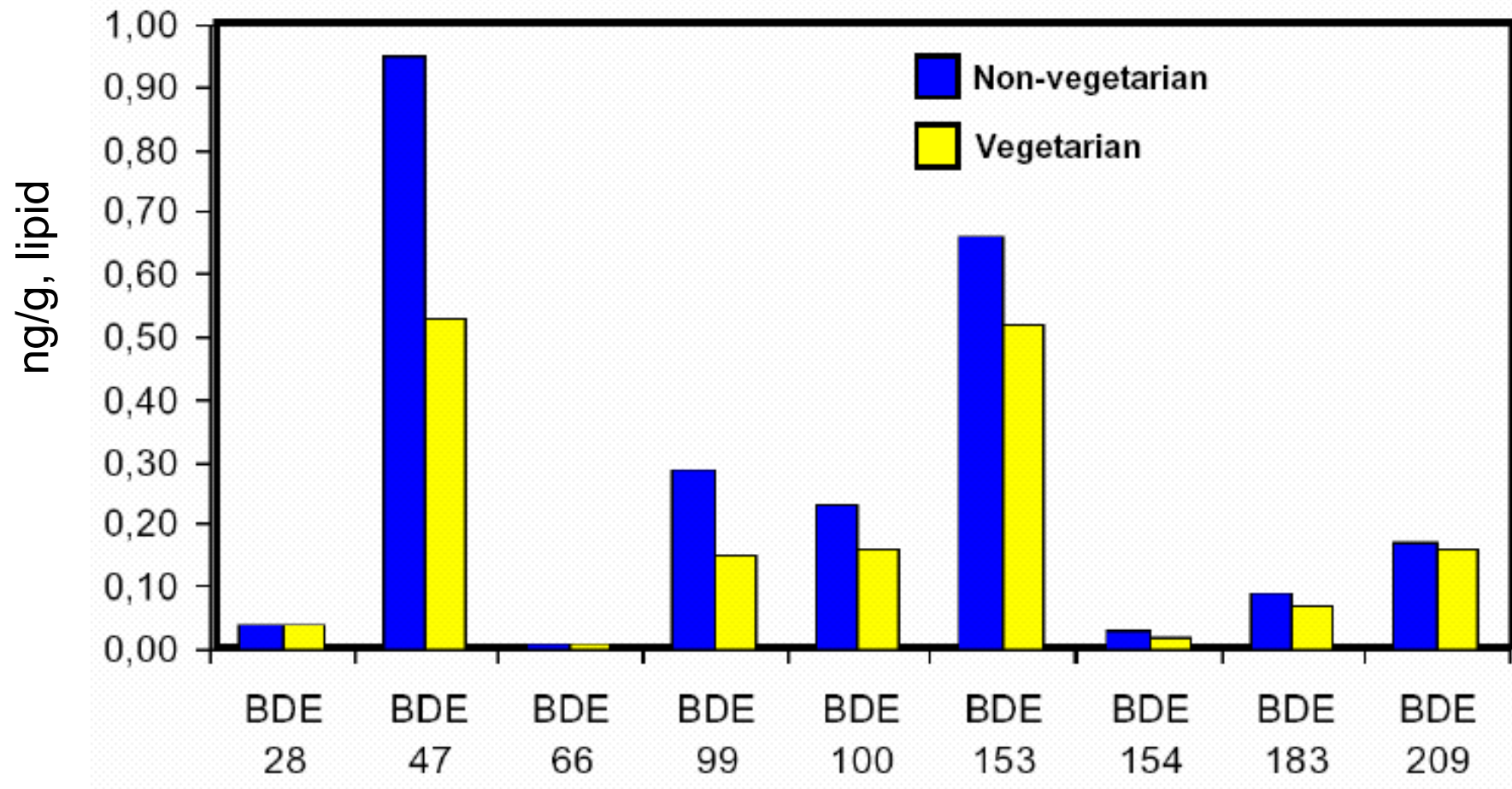
Paepke *et al.*



$r = -0.6$, $p > 0.05$

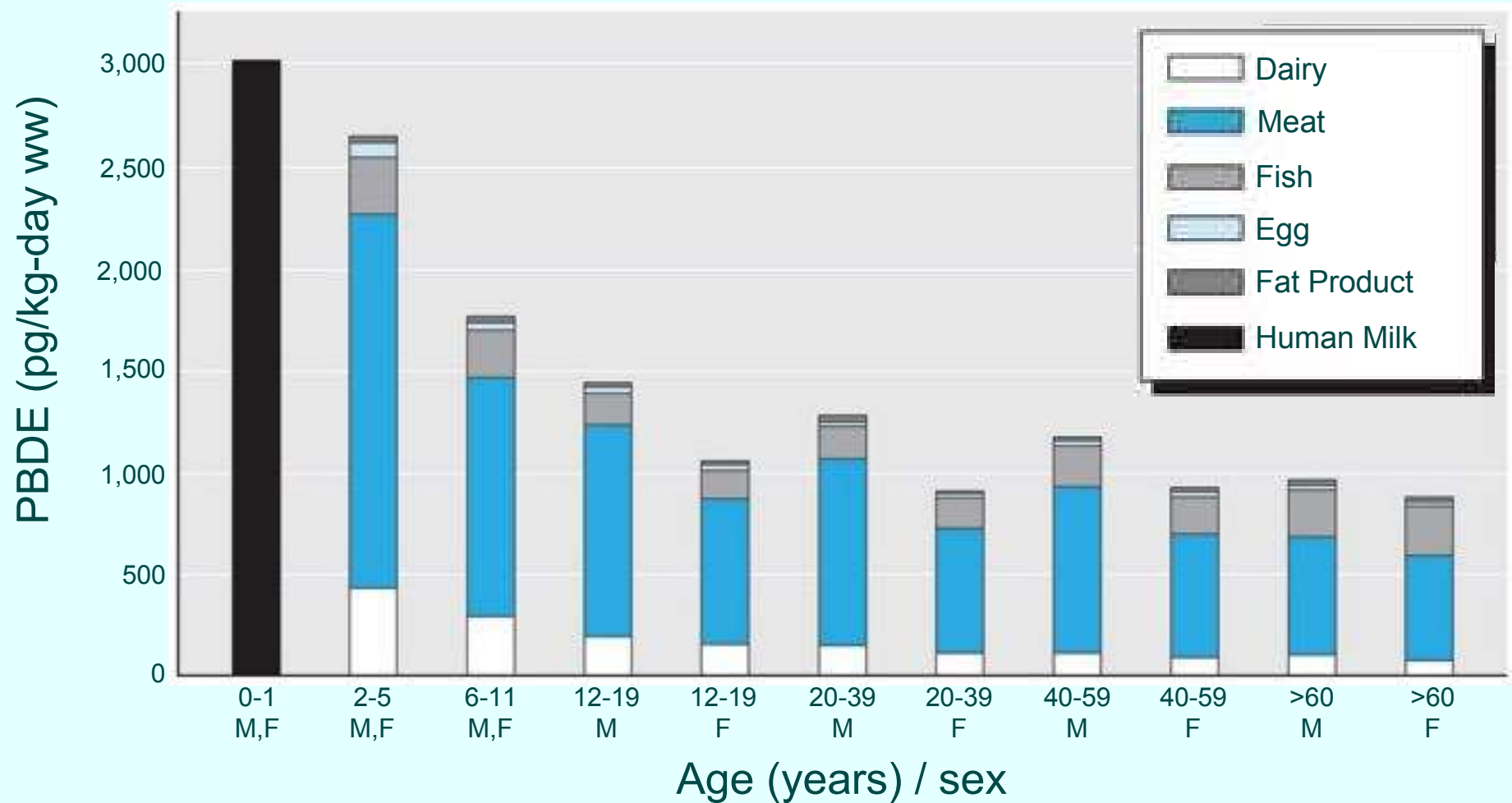
Schechter *et al.*

Comparison of PBDE Levels in Human Milk Non-Vegetarians vs. Vegetarians



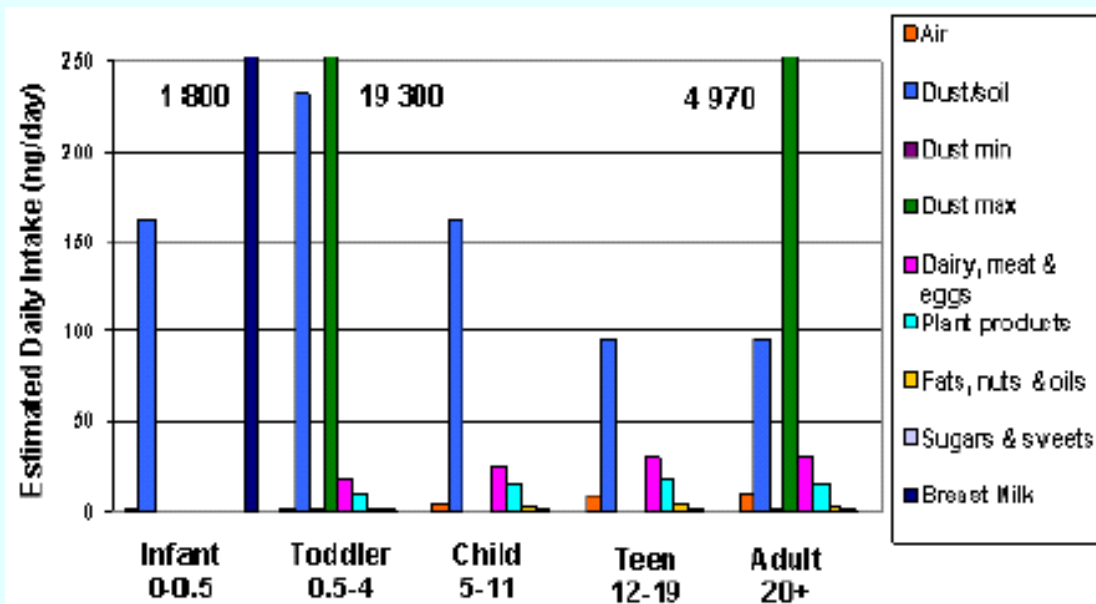
Paepke *et al.*

Daily PBDE Dietary Intake of U.S. Population

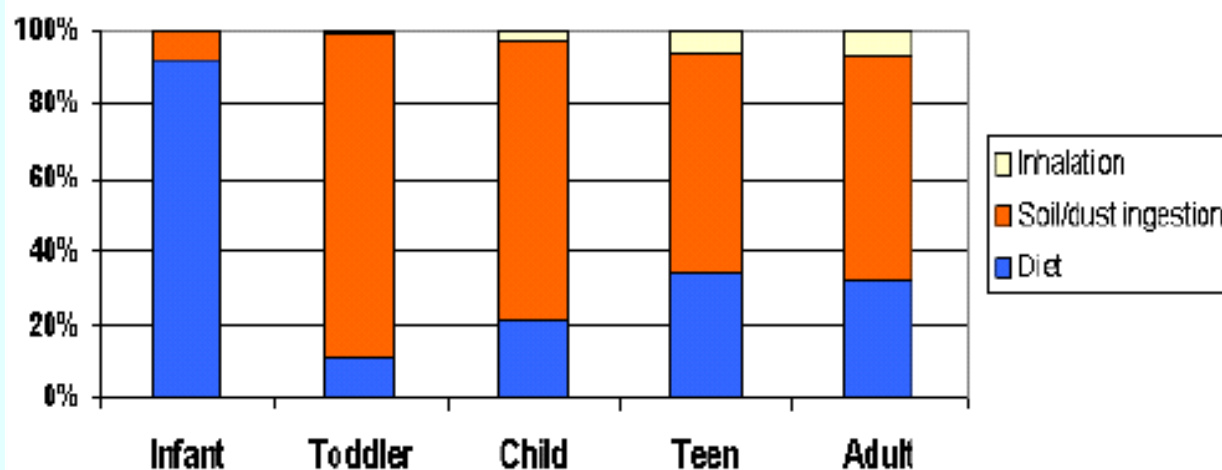


Schechter *et al.*, Environ. Health Perspect., 2006

Relative Contribution From Different Pathways Canada



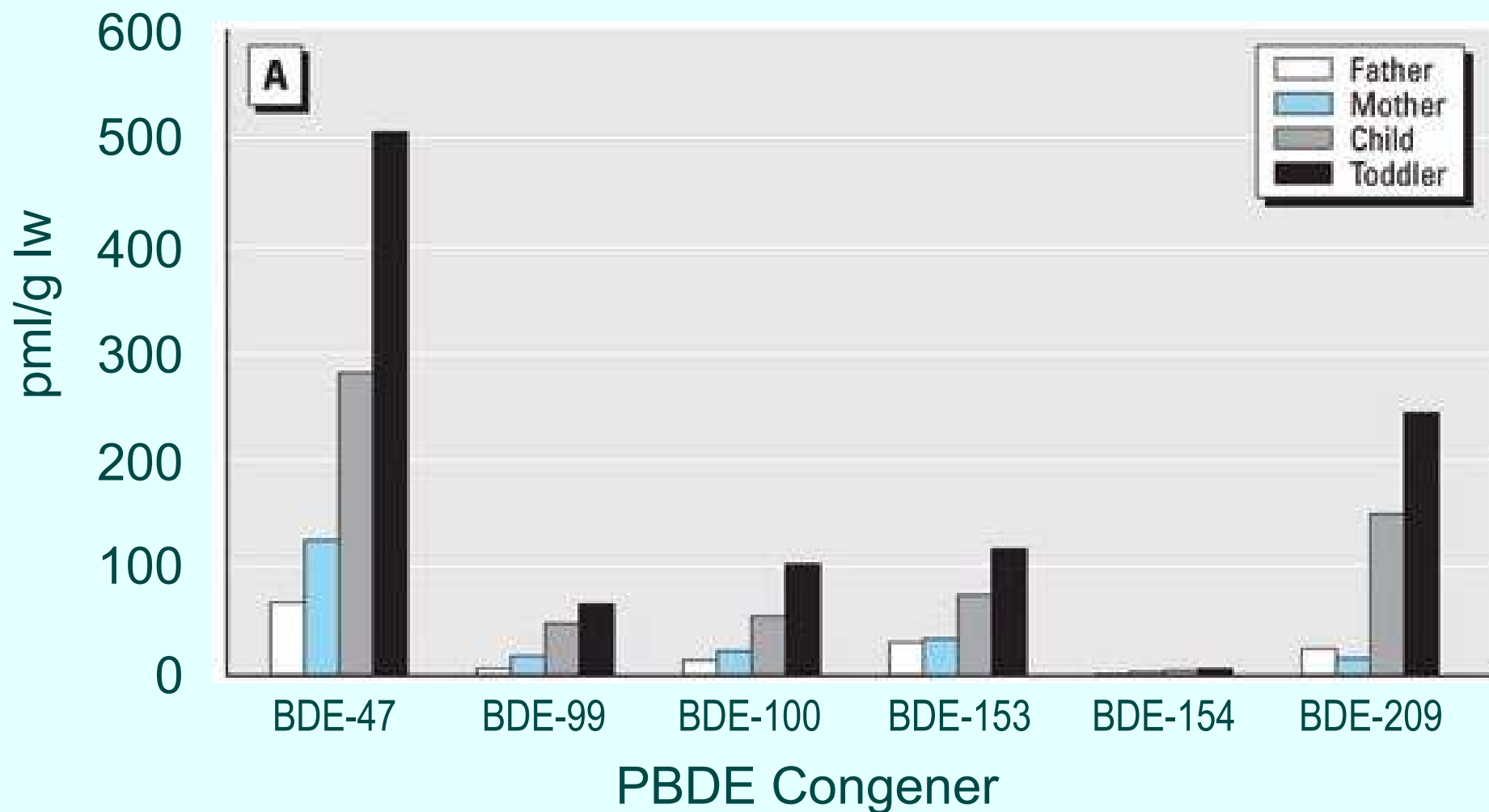
Estimated Daily Intake of total PBDEs for “average” Canadian age classes and minimum and maximum intakes of dust for toddlers and adults



% contributions from inhalation, soil/dust ingestion and diet to “average” Canadian exposure to total PBDEs

Jones-Otazo *et al.*, 2005

PBDE Concentrations in Serum Samples



Fischer *et al.*, Environ. Health Perspect., 2006

Conclusions

- ◆ PBDE levels in U.S. population's blood and milk is 10-20 times higher than European levels, yet U.S. food levels not than higher than European levels.
- ◆ Diet may not be a major source of exposure.
- ◆ In contrast, >95% of general populations exposure to PCBs and dioxins came from food.
- ◆ Possible there exists other routes of PBDE entry to the body; e.g. dust intake.

Schechter *et al.*, BFR 2006

Toxicity of PBDEs

Toxic Effects of PBDEs

◆ Decreased thyroid hormone

- 47, 99, 100, 153, various mixtures in several studies
- decaBDE following postnatal exposure (Rice *et al.*, submitted)
- decaBDE produced thyroid follicular cell hyperplasia in 2-year cancer assay

◆ Reproductive hormones and function

- 47, 99, 153, commercial mixtures
- decaBDE active after photoactivation

◆ Developmental neurotoxicity

Toxic Effects of PBDEs

- ◆ Suppression of immune function
 - various commercial mixtures, 47
 - others not studied
- ◆ Induction of hepatic enzymes
- ◆ Carcinogenicity
 - decaBDE only congener assessed
 - carcinogenic in two species and multiple organs

Developmental Neurotoxicity of PBDEs

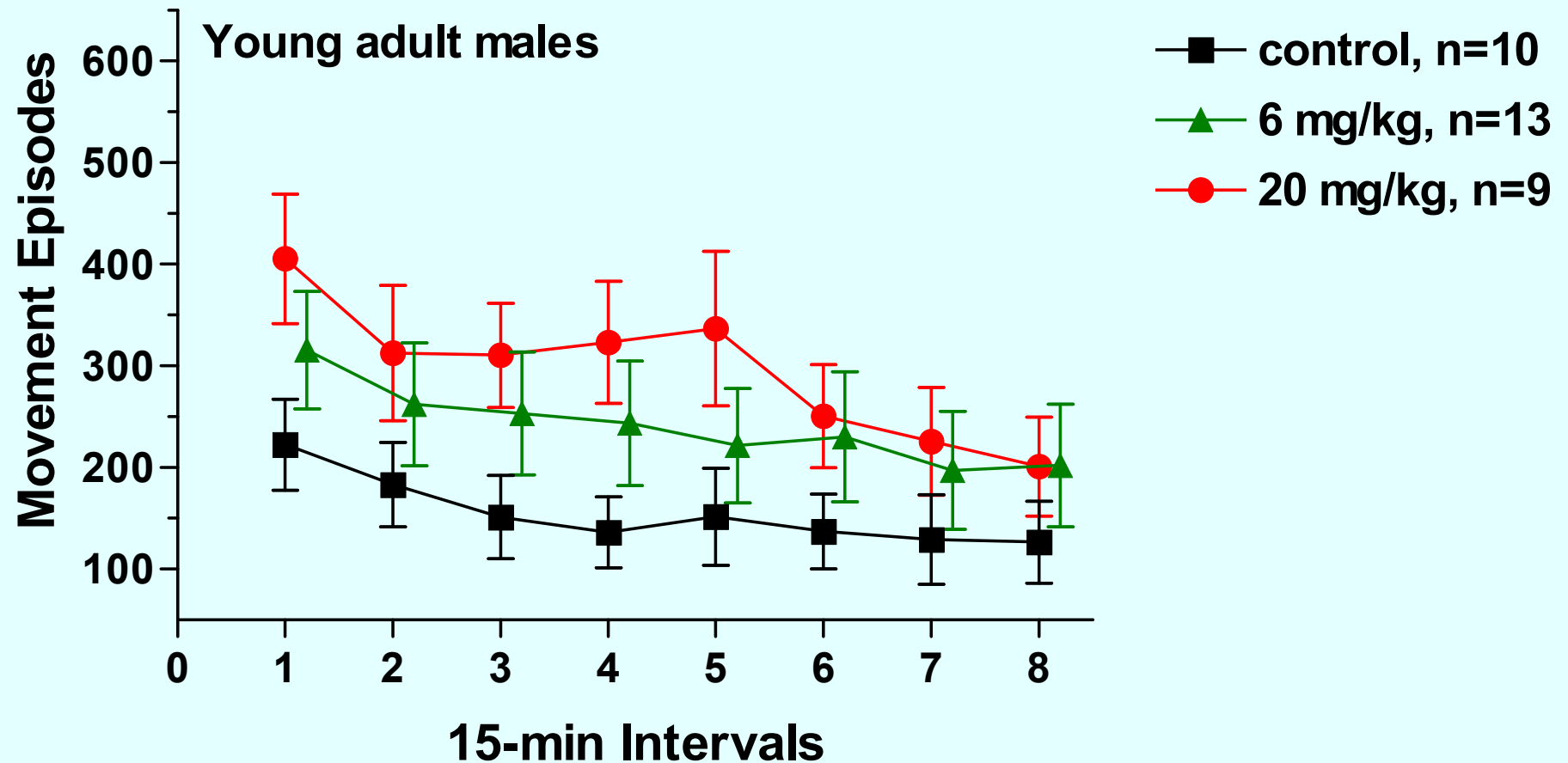
- ◆ Swedish group studied motor activity in mice dosed on postnatal day 3, 10, or 19
 - congeners 47, 99, 153, 183, 203, 206, and 209 all produced similar effects on motor activity
 - effects on learning observed with 203, 206, or 153 but not 183
 - PCB + BDE are additive in producing motor effects
 - decaBDE + PFOA also interacted
 - BDE-99 or PCBs interact with methylmercury (Fischer *et al.*, 2006)
- ◆ Congeners 47, 99, 153, 183, 203, 206 are all potential breakdown products or metabolites of 209 (deca)

University of Southern Maine/Maine CDE DecaBDE Study

- ◆ Mice exposed on postnatal days 2-15 with 6 or 20 mg/kg/day
 - female and male littermates assessed preweaning, young adulthood, one year of age
- ◆ **Functional Observation Battery**
 - development of sensorimotor integration
 - retarded development of grip strength and palpebral (blink) reflex
- ◆ Increased activity in males in early adulthood
- ◆ Increased errors on a learning task
- ◆ Decreased thyroid levels after weaning

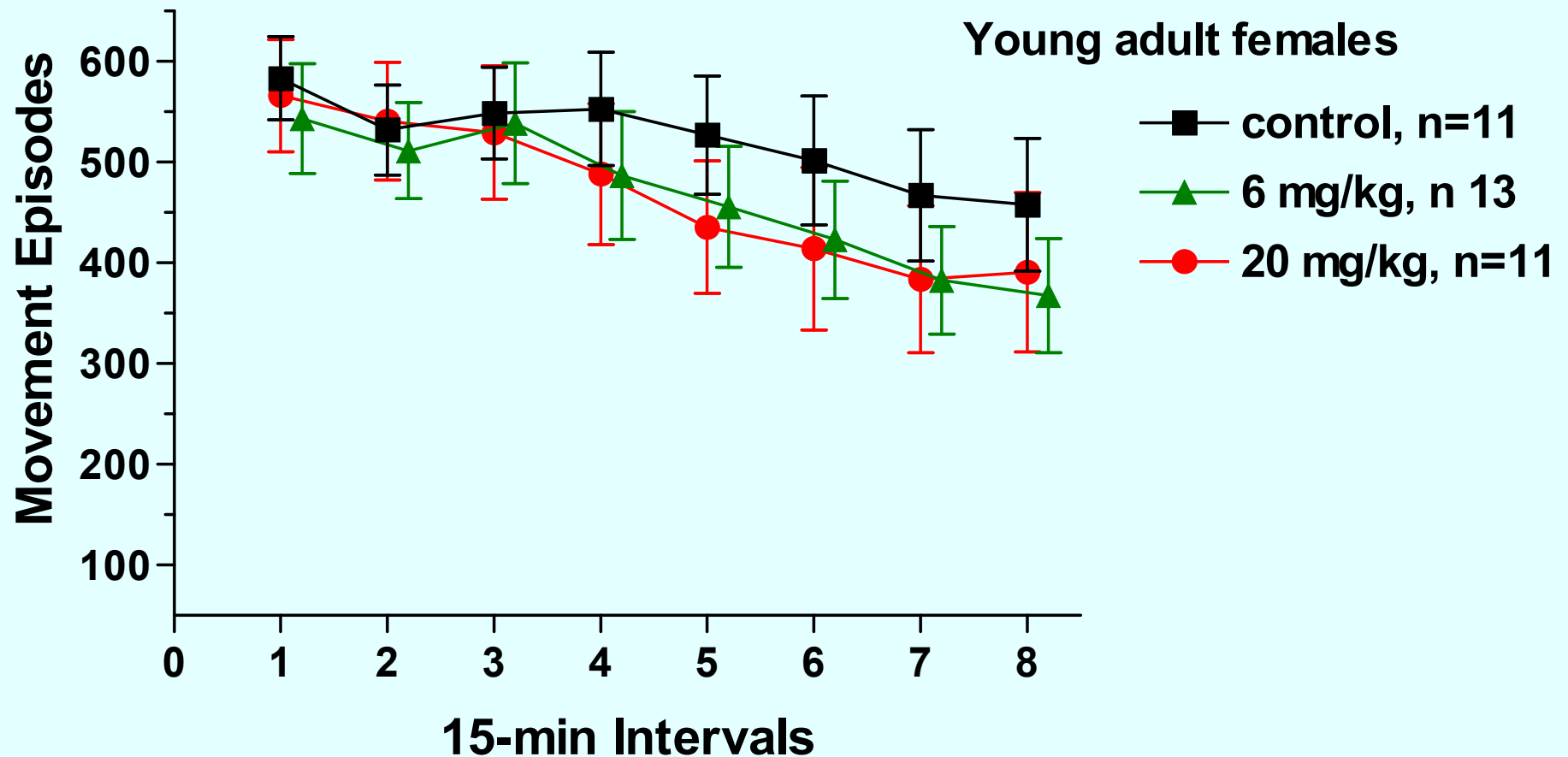
University of Southern Maine/Maine CDC DecaBDE Study

2-hr Activity Assay



University of Southern Maine/Maine CDC DecaBDE Study

2-hr Activity Assay



Possible PBDE Effects in Humans

Chao *et al.*, 2006

- ◆ Association between birth outcome and 12 PBDE congeners in breast milk
- ◆ DecaBDE levels predicted lower birth weight and length, smaller head circumference
 - five other congeners associated with one or more of these endpoints
- ◆ DecaBDE associated with decreased cycle length and decreased duration of menstrual bleeding before covariate adjustment (n = 20)
 - 100 and 153 also associated with decreased cycle length
- ◆ Correlations among congeners was not presented, making interpretation difficult with respect to individual congeners

Chemical Alternatives to DecaBDE

Maine DEP

- ◆ Other brominated compounds
 - those currently in use are PBTs
 - TBBPA, HBCD
- ◆ TV casings (80% of decaBDE use)
 - bisphenol A diphosphate (BAPP)
 - releases bisphenol A, a potent endocrine disruptor
 - Resorcinol bis diphenylphosphate (RDP)
 - triphenyl phosphate is toxic to mammals
 - RDP toxic to aquatic organisms
 - German Federal Environment Agency considers that there are insufficient data for determination of suitability

Chemical Alternatives to Deca BDE

Maine DEP

◆ Circuit boards, wiring

- alkyl phosphonic acid - almost no information
- red phosphorus, ammonium polyphosphate, magnesium hydroxide
- little known but presumably non-toxic

◆ Melamine cyanurate

- little information
- GFEA considers data insufficient for determination of suitability

decaBDE: A Cautionary Tale

◆ Assertion

- deca BDE will not be persistent or transported
- big molecule, low volatility

◆ Reality

- transported long distances, degraded in the environment to toxic congeners

◆ Assertion

- decaBDE will not be absorbed, and will not bioconcentrate

◆ Reality

- decaBDE is absorbed, metabolites and possibly parent can bioconcentrate, present in human food chain

◆ Assertion

- decaBDE is not toxic

◆ Reality

- may be largely true for parent compound based on *in vitro* studies
- toxic to multiple systems *in vivo*
- metabolites and degradation products are toxic